********** STN Columbus **********

FILE 'HOME' ENTERED AT 13:51:53 ON 25 JUL 2000

=> file medline

COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.15 0.15

FILE 'MEDLINE' ENTERED AT 13:52:00 ON 25 JUL 2000

FILE LAST UPDATED: 20 JUL 2000 (20000720/UP). FILE COVERS 1960 TO DATE.

MEDLINE has been reloaded to reflect the annual MeSH changes made by
the National Library of Medicine for 2000. Enter HELP RLOAD for details.

OLDMEDLINE, data from 1960 through 1965 from the Cumulated Index
Medicus (CIM), has been added to MEDLINE. See HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the
Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
SUBSTANCE IDENTIFICATION.

=> breeding/ab,bi

BREEDING IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s breeding/ab,bi

16359 BREEDING/BI
5361026 AB/FA
8963 BREEDING/AB
(BREEDING/BI (L) AB/FA)
16359 BREEDING/BI
L1 16359 BREEDING/AB,BI

=> s l1 and balb?/ab,bi

69950 BALB?/BI
5361026 AB/FA
22759 BALB?/AB
(BALB?/BI (L) AB/FA)
69950 BALB?/BI
L2 139 L1 AND BALB?/AB,BI

=> s l2 and trait#/ab,bi

25416 TRAIT#/BI
5361026 AB/FA
20788 TRAIT#/AB
(TRAIT#/BI (L) AB/FA)
25416 TRAIT#/BI
L3 5 L2 AND TRAIT#/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 5 MEDLINE
AN 1999178270 MEDLINE
DN 99178270
TI High-resolution mapping of quantitative ***trait*** loci in outbred
mice.
AU Talbot C J; Nicod A; Cherny S S; Fulker D W; Collins A C; Flint J
CS Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, UK.
SO NATURE GENETICS, (1999 Mar) 21 (3) 305-8.
Journal code: BRO. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
EW 19990601
AB Screening the whole genome of a cross between two inbred animal strains
has proved to be a powerful method for detecting genetic loci underlying
quantitative behavioural ***traits*** , but the level of resolution
offered by quantitative ***trait*** loci (QTL) mapping is still too
coarse to permit molecular cloning of the genetic determinants. To achieve
high-resolution mapping, we used an outbred stock of mice for which the
entire genealogy is known. The heterogeneous stock (HS) was established 30
years ago from an eight-way cross of C57BL/6, ***BALB*** /c, RIII, AKR,
DBA/2, I, A/J and C3H inbred mouse strains. At the time of the experiment
reported here, the HS mice were at generation 58, theoretically offering
at least a 30-fold increase in resolution for QTL mapping compared with a
backcross or an F2 intercross. Using the HS mice we have mapped a QTL
influencing a psychological ***trait*** in mice to a 0.8-cM interval
on chromosome 1. This method allows simultaneous fine mapping of multiple
QTLs, as shown by our report of a second QTL on chromosome 12. The high
resolution possible with this approach makes QTLs accessible to positional
cloning.

L3 ANSWER 2 OF 5 MEDLINE
AN 97124847 MEDLINE
DN 97124847
TI Frequent DNA polymorphisms exist in inbred CBA/J and C3H/HeN mice.
AU Yuan B; Shum-Siu A; Lentsch E M; Hu L H; Hendler F J
CS Department of Biochemistry, J. Graham Brown Cancer Center, University of
Louisville, Kentucky 40292, USA.
SO GENOMICS, (1996 Nov 15) 38 (1) 58-71.
Journal code: GEN. ISSN: 0888-7543.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M21390; GENBANK-V00829; GENBANK-X01799; GENBANK-Y00309;
GENBANK-D00439; GENBANK-M34098; GENBANK-X14061; GENBANK-M84387;
GENBANK-M36332; GENBANK-X13781; GENBANK-M26284; GENBANK-M12099;
GENBANK-M22065; GENBANK-M17922; GENBANK-X07197; GENBANK-X56007;
GENBANK-M31941; GENBANK-X06856; GENBANK-S69706; GENBANK-X07439;
GENBANK-M24410; GENBANK-A01690; GENBANK-J03820; GENBANK-X05064;
GENBANK-X03020; GENBANK-M25149; GENBANK-X06762; GENBANK-X02801
EM 199705
EW 19970504
AB Although occasional DNA polymorphisms have been observed in inbred mice,
CBA/J and C3H/HeN mice have two microsatellite alleles at over 1/3 of
microsatellite loci tested. Since DNA polymorphisms were not detected in
DBA/2J, C57BL/6J, and ***BALB*** /cJ, the frequency of microsatellite
polymorphisms appears to be strain specific. Thus, genetic studies in
inbred mice require testing for preexisting polymorphisms. The
polymorphisms detected in CBA/J mice appear to be stable and do not

represent microsatellite instability or a mutator phenotype. Somatic mosaicism was not observed and no more than two alleles were detected per locus. CBA/J propagated only by brother-sister mating maintained seven of eight polymorphisms over 5 years. These data suggest that the polymorphisms are due to an inherited ***trait*** and that the pattern of inheritance is not due to Mendelian distribution. As ***breeding*** analysis was not performed, the pattern of allelic inheritance is unknown.

L3 ANSWER 3 OF 5 MEDLINE
AN 95361094 MEDLINE
DN 95361094
TI Genetic susceptibility to papilloma progression in SENCAR mice.
AU Stern M C; Gimenez-Conti I B; Conti C J
CS Department of Carcinogenesis, University of Texas M.D. Anderson Cancer Center, Smithville, USA..
NC CA53123 (NCI)
CA57596 (NCI)
SO CARCINOGENESIS, (1995 Aug) 16 (8) 1947-53.
Journal code: C9T. ISSN: 0143-3334.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199511
AB Previous results showed that in an inbred line (SSIN) derived from outbred SENCAR mice there is a dissociation between susceptibility to papilloma development and the malignant conversion of these into squamous cell carcinomas (SCC). To extend this conclusion, we designed an interstrain ***breeding*** experiment using the two-step carcinogenesis protocol in order to study the susceptibility to tumor progression of F1 offspring. The strains used were SSIN, ***BALB*** /c, both known for their resistance to papilloma progression, and SENCAR. Both the SSIN X SENCAR and SENCAR X SSIN F1s showed a promotion sensitivity similar to that of the SSIN mice. This behavior was also seen in the SSIN X (SSIN X SENCAR) and SSIN X (SENCAR X SSIN) backcrossed animals, suggesting that susceptibility to 12-O-tetradecanoylphorbol-13-acetate promotion under these protocol conditions is inherited as a dominant ***trait*** . The ***BALB*** /c X SENCAR F1s showed an average response that was intermediate between the two parental strains/stocks. Regarding the progression, all F1s showed a cumulative number of SCCs similar to the SENCAR progenitor. We also investigated the previously described switch of keratin 1 to 13 as a marker of premalignant progression, which is significatively delayed in SSIN mice compared with SENCAR mice. The SSIN X SENCAR F1s expressed this switch in a way similar to the SENCAR mice. These findings suggest that susceptibility to tumor progression is inherited as a dominant autosomal ***trait*** . The putative gene(s) that confers susceptibility is present in the SENCAR stock and was probably lost in the selection and inbreeding of the SSIN mice.

L3 ANSWER 4 OF 5 MEDLINE
AN 84214114 MEDLINE
DN 84214114
TI Susceptibility of inbred mice to Leishmania tropica infection: genetic control of the development of cutaneous lesions in P/J mice.
AU Fortier A H; Meltzer M S; Nacy C A
SO JOURNAL OF IMMUNOLOGY, (1984 Jul) 133 (1) 454-9.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198409
AB Leishmania tropica infections of P/J mice are characterized by the development of progressive nonhealing cutaneous lesions, followed by visceral metastases to liver and spleen. To analyze the genetic control of this disease, we produced F1, backcross (BX), and F2 progeny by ***breeding*** susceptible P/J mice with L. tropica-resistant C3H/HeN mice. Infections in these hybrid animals suggested that genetic control of the cutaneous lesion was by a single, autosomal, dominant gene. Resistance was the dominant ***trait*** . Analysis of liver and spleen impression smears in these animals, however, indicated that development of the cutaneous lesion segregates independently of the second component of L. tropica infections, systemic disease.

L3 ANSWER 5 OF 5 MEDLINE
AN 77005234 MEDLINE
DN 77005234
TI Inherited resistance to Corynebacterium kutscheri in mice.
AU Hirst R G; Wallace M E
SO INFECTION AND IMMUNITY, (1976 Aug) 14 (2) 475-82.
Journal code: GO7. ISSN: 0019-9567.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197701
AB An analysis of the factors responsible for inherited resistance to Corynebacterium kutscheri was undertaken. Various inbred mouse strains were examined; these included the Swiss Lynch and C57Bl/l mice, their F1 and F2 progeny, and the progeny of the F1 backcrossed to each parent strain. Two modes of inherited resistance are described. An examination suggested that resistance as measured by the mean lethal dose of C. kutscheri was under polygenic control and was inherited continuously. However, the efficiency with which C. kutscheri was eliminated by the mononuclear phagocyte cells of the liver over 3 days differed markedly among strains. A genetic analysis of this mononuclear phagocyte microbicidal efficiency (MPME) in Swiss Lynch and C57Bl/6 mice was undertaken. The ***trait*** , MPME, was present, but did not segregate, in the F1 progeny or in the progeny of the backcross to the resistant C57Bl/6 parent; this was clear evidence of dominance. Moreover, MPME segregated in a ratio of 1:1 in the progeny of the backcross to the sensitive Swiss Lynch parent and in a ratio of 3:1 in the F2 progeny. It was concluded that MPME was inherited discontinuously and was controlled by a single dominant autosomal gene (or closely linked group); the recessive allele was assigned the gene symbol ack. Linkage experiments showed there to be no association between the ack locus and any of the immune-response genes.

=> s rheumatoid arthritis/ab,bi

62441 RHEUMATOID/BI
84571 ARTHRITIS/BI
5361026 AB/FA
23124 RHEUMATOID ARTHRITIS/AB
((RHEUMATOID(W)ARTHRITIS)/BI (L) AB/FA)
62441 RHEUMATOID/BI
84571 ARTHRITIS/BI
35308 RHEUMATOID ARTHRITIS/BI
((RHEUMATOID(W)ARTHRITIS)/BI)
L4 35308 RHEUMATOID ARTHRITIS/AB,BI

=> s l4 and breed?/ab,bi

24083 BREED?/BI
5361026 AB/FA
16681 BREED?/AB
(BREED?/BI (L) AB/FA)
24083 BREED?/BI
L5 9 L4 AND BREED?/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 9 MEDLINE
AN 1999142388 MEDLINE
DN 99142388
TI Organization of the canine major histocompatibility complex: current perspectives.
AU Wagner J L; Burnett R C; Storb R
CS Fred Hutchinson Cancer Research Center, Program in Transplantation Biology, Seattle, WA 98109-1024, USA.
NC CA31787 (NCI)
CA18221 (NCI)
RR12558 (NCRR)
+
SO JOURNAL OF HEREDITY, (1999 Jan-Feb) 90 (1) 35-8. Ref: 29
Journal code: IC7. ISSN: 0022-1503.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199905
EW 19990503
AB The dog is a valuable model for studying several human diseases as well as one of the most important models for organ transplantation. Important to understanding the pathophysiology or development of some of these diseases is an understanding of the canine major histocompatibility complex (MHC) or dog leukocyte antigen (DLA). Initial characterization of the DLA involved primarily cellular, serological, and biochemical analyses. Later a molecular analysis of the DLA region was begun. There are at least four complete class I genes: DLA-88, DLA-12, DLA-64, and DLA-79. DLA-88 is highly polymorphic, with more than 40 alleles obtained from an examination of 50 mixed ***breed*** dogs. The other class I loci are less polymorphic, with fewer than 12 alleles each. In the class II region there is one complete DRB gene called DLA-DRB1 with at least 24 alleles and one full-length DQB gene, DLA-DQB1, with 20 alleles characterized to date. DLA-DQA is less polymorphic with nine alleles and DLA-DRA appears monomorphic. Two highly polymorphic canine microsatellite markers, one located in the class I region and one located in the class II region, can be used to identify DLA-matched and -mismatched dogs within families for organ transplantation experiments. Future projects include mapping the DLA region by pulsed-field gel electrophoresis and using a recently constructed canine bacterial artificial chromosome (BAC) library to search for new genes within the DLA. The dog has been a useful model for understanding several human diseases such as gluten-sensitive enteropathy (Hall and Batt 1990), ***rheumatoid*** ***arthritis*** (Halliwell et al. 1972), narcolepsy (Tafti et al. 1996), and systemic lupus erythematosus (Lewis and Schwartz 1971, Teichner et al. 1990), as well as an important model for solid organ and hematopoietic stem cell transplantation (Storb and Deeg 1985). Much of the impetus behind efforts to characterize the canine MHC comes from its importance in transplantation. In spite of the dog's importance in studying human disease and in immunology, molecular analysis of the DLA has lagged behind that of the mouse and human as well as several agricultural animals.

L5 ANSWER 2 OF 9 MEDLINE
AN 97376834 MEDLINE
DN 97376834
TI High affinity rheumatoid factor transgenic B cells are eliminated in normal mice.
AU Wang H; Shlomchik M J
CS Department of Laboratory Medicine, Yale University School of Medicine, New Haven, CT 06520, USA.
NC P01 AI/ AR36529 (NIAID)
SO JOURNAL OF IMMUNOLOGY, (1997 Aug 1) 159 (3) 1125-34.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199710
EW 19971003
AB Although systemic autoimmune diseases can be accompanied by multiple autoantibodies, certain specificities are dominant. Presumably, these specificities and their cognate Ags have properties that make them particularly amenable to autoimmune induction. Rheumatoid factors (RFs) are a dominant class of autoantibodies in ***rheumatoid*** ***arthritis*** and certain other autoimmune syndromes. To study the regulation of RFs in normal and autoimmune animals, we previously created a RF Ig transgenic model based on an RF isolated from an autoimmune MRL/lpr mouse. Using this model, called AM14, we were surprised to find that normal mice do not regulate disease-related RF B cells. This raised the question of whether RFs in general are not susceptible to tolerance induction, perhaps due to the unique properties of serum IgG and its FcRs. Alternatively, RFs can be tolerized, and the disease-related RFs are below the affinity threshold for such tolerance. To distinguish these possibilities, we generated a second RF transgenic model with the same specificity but much higher affinity than AM14. We found that, in contrast to AM14, high affinity RF B cells are subject to central tolerance, showing that there is not an absolute defect in RF B cell tolerance, but, rather, that RF B cell tolerance is affinity dependent even in normal animals. This is also the first model in which a disease-related specificity has been shown clearly to delete in a system in which Ag-positive and negative mice can be produced and compared.

L5 ANSWER 3 OF 9 MEDLINE
AN 95142883 MEDLINE
DN 95142883
TI The viable motheaten (mev) mouse--a new model for arthritis.
AU Kovarik J; Kuntz L; Ryffel B; Borel J F
CS Immunology Department, Sandoz Pharma Ltd, Basel, Switzerland.
SO JOURNAL OF AUTOIMMUNITY, (1994 Oct) 7 (5) 575-88.
Journal code: ADL. ISSN: 0896-8411.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199505
AB Homozygous mev mice are first identified at the age of 3-4 days by focal depigmentation of the skin, followed by patchy absence of hair and

by
necrotic lesions on paws, tail and ears. Of particular interest are the inflammatory reactions in the paws of these animals which consist mainly
of polymorphonuclear and mononuclear cell infiltration in the subcutaneous
tissue extending to the periosteum and joint, resulting in focal destructive arthritis and osteomylitis. These lesions are to some extent
reminiscent of an acute form of rheumatoid-like arthritis. Since mev mice
are sterile, a limited number of symptomatic offspring can be obtained by
cross- ***breeding*** their heterozygous siblings which are phenotypically not distinguishable from mice lacking this mutation. In
order to produce a sufficient number of diseased animals for performing
pharmacological studies, we have established a model by transferring this
disease in lethally irradiated, 8- to 10-week-old syngeneic mice which
were grafted with mev spleen cells. Such reconstituted recipients develop
first inflammatory symptoms of the paws 2 to 3 weeks after cell transfer.
The arthritic inflammation finally affects all paws and toes by 30 to 50
days. This procedure increased the number of mev-like mice expressing
arthritis, allowing assessment of the effects of standard reference drugs
used in the therapy of ***rheumatoid*** ***arthritis*** (RA). The
immunosuppressants cyclosporin and rapamycin and the steroid dexamethasone
at therapeutic concentrations exert a strong inhibitory effect on the development of arthritis in this novel model. In contrast, the
non-steroidal anti-inflammatory drug phenylbutazone shows only a moderate
effect. These results indicate the particular sensitivity of this model for efficacy of potentially new therapeutic but non-cytostatic compounds
for clinical use.

L5 ANSWER 4 OF 9 MEDLINE
AN 93375854 MEDLINE
DN 93375854
TI Magnetic resonance microscopy in rat skeletal research.
AU Kapadia R D; High W B; Soulleveld H A; Bertolini D; Sarkar S K
CS Department of Physical & Structural Chemistry, SmithKline Beecham
Pharmaceuticals, King of Prussia, Pennsylvania..
SO MAGNETIC RESONANCE IN MEDICINE, (1993 Aug) 30 (2) 247-50.
Journal code: MHR. ISSN: 0740-3194.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199312
AB Noninvasive evaluation of skeletal tissue, particularly certain sites that
tend to be predisposed to disease, is critical in understanding the pathogenesis, progression, and successful treatment of various diseases
like osteoporosis, ***rheumatoid*** ***arthritis*** , and
osteoarthritis. Although several noninvasive techniques are currently
available to evaluate skeletal tissues, they all have critical limitations. We report here a systematic study to compare the
morphological changes (overall profile and tissue architecture) in the
proximal tibiae and coccygeal vertebrae of a young growing rat and an
older retired female ***breeder*** rat using 2- and 3-dimensional MR
(magnetic resonance) microscopy and histology. We have obtained MR
microimages of intact rat tibiae and vertebrae with resolution upto 24 24
250 microns and have found excellent correlations between MR microscopy
results and histological assessment.

L5 ANSWER 5 OF 9 MEDLINE
AN 91224865 MEDLINE
DN 91224865
TI Juvenile-onset polyarthritis syndrome in Akitas.
AU Dougherty S A; Center S A; Shaw E E; Erb H A
CS Department of Clinical Science, New York State College of Veterinary
Medicine, Cornell University, Ithaca 14853-6401..
SO JOURNAL OF THE AMERICAN VETERINARY MEDICAL ASSOCIATION, (1991 Mar 1) 198
(5) 849-56.
Journal code: HAV. ISSN: 0003-1488.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199108
AB Two young Akitas were examined because of manifestation of a juvenile-onset form of polyarthritis. A search of medical records at the
New York State College of Veterinary Medicine found 6 more similarly
affected Akitas. The clinical manifestations were marked by cyclic febrile
illness and signs of profound joint-related pain. Two dogs had concurrent
aseptic meningitis. The syndrome resembles juvenile ***rheumatoid*** ***arthritis*** in human beings, although it shares features with systemic lupus erythematosus. Pedigree analysis of affected Akitas supported a heritable component to the syndrome. Treatment with immunosuppressive drugs was effective in 2 dogs that achieved complete
remission, and in 2 dogs that achieved only partial remission. Classification of this syndrome is difficult and may represent an "overlap" syndrome commonly described in human beings.

L5 ANSWER 6 OF 9 MEDLINE
AN 86193107 MEDLINE
DN 86193107
TI Update on ibuprofen: review article.
AU Busson M
SO JOURNAL OF INTERNATIONAL MEDICAL RESEARCH, (1986) 14 (2) 53-62. Ref: 58
Journal code: E62. ISSN: 0300-0605.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 198608
AB Non-steroidal anti-inflammatory drugs (NSAIDs) have become the principal
mode of therapy for rheumatic diseases and their use has continued to
increase despite concern expressed recently regarding potential hazards
(Figure 1). Prior to 1969, a limited number of NSAID drugs were available.
Aspirin and indomethacin became the mainstay of treatment but tolerability, particularly gastric irritation, at doses necessary to control rheumatic symptoms limited the usefulness of these valuable
agents. The pyrazolone, phenylbutazone, showed slightly better gastro-intestinal (GIT) tolerability but has since been associated with an
increased risk of blood dyscrasiae and is now only available for restricted use in most countries. Ibuprofen was the first of a new ***breed*** of NSAIDs originally introduced into the United Kingdom in
1969. Chemically quite distinct from its forerunners it was the first of
the propionic acid derivatives to be used in rheumatic practice. The propionics have since become the largest, single and most important group
of NSAIDs accounting for 50% of NSAID prescriptions in the United Kingdom.
It is estimated that over 100 million patients worldwide have received
ibuprofen which is now available in over 100 countries throughout the
world including all the major markets. Ibuprofen was developed directly as
a result of the problems associated with the use of corticosteroids in

the
treatment of ***rheumatoid*** ***arthritis*** and also because of
the gastro-intestinal irritation and general intolerability of the
established NSAIDs, at that time. Ibuprofen was readily accepted because,
unlike the previous drugs, its therapeutic efficacy was easily seen to
outweigh the severity of its side-effects. Ibuprofen was the first new
drug with the potency of aspirin but without its major disadvantages.

L5 ANSWER 7 OF 9 MEDLINE
AN 85225766 MEDLINE
DN 85225766
TI Induction of chronic polyarthritis in rabbits by hyperimmunization with
Escherichia coli. I. Pathologic and serologic features in two
breeds of rabbits.
AU Aoki S; Ikuta K; Nonogaki T; Ito Y
SO ARTHRITIS AND RHEUMATISM, (1985 May) 28 (5) 522-8.
Journal code: 90M. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198509
AB Hyperimmunization of 147 rabbits (outbred Japanese white rabbits and New
Zealand white [NZW] rabbits bred in a closed colony) with heat-killed
Escherichia coli 0:14 in Freund's incomplete adjuvant resulted in the
animals developing a chronic polyarthritis resembling ***rheumatoid***
arthritis (RA). While both Japanese white and NZW rabbits showed a
high incidence of the induced arthritis, a higher proportion of NZW
rabbits developed the disease, suggesting that genetic influence is
important in the development of RA-like illness. This experimental model
may be useful for the study of RA.

L5 ANSWER 8 OF 9 MEDLINE
AN 76259841 MEDLINE
DN 76259841
TI Noninfectious canine arthritis: ***rheumatoid*** ***arthritis*** .
AU Pedersen N C; Castles J J; Weisner K
SO JOURNAL OF THE AMERICAN VETERINARY MEDICAL ASSOCIATION, (1976 Aug 1) 169
(3) 295-303.
Journal code: HAV. ISSN: 0003-1488.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197612
AB Chronic unremitting, generally symmetric, erosive polyarthritis was
studied in 8 dogs. The disease had clinical, serologic, radiographic, and
pathologic changes similar to those of ***rheumatoid*** ***arthritis*** of man. The condition occurred mainly in smaller
breeds of dogs, with time of onset from 8 months to 8 years of
age, Characteristic radiographic changes were seen in the joints several
weeks to several months after the appearance of the initial lameness.
Synovial fluid contained an increased number of neutrophils, and synovial
fluid and synovial tissues were sterile for anaerobic and aerobic
bacteria, mycoplasma, chlamydia, and viruses. Corticosteroids were
therapeutically ineffective in all of the cases; however, corticosteroids,
cyclophosphamide, and azathioprine were effective when used in combination
in several dogs.

L5 ANSWER 9 OF 9 MEDLINE
AN 76201375 MEDLINE
DN 76201375
TI [The significance of immunologic phenomenons in pulmonary diseases of
children (author's transl)].
Die Bedeutung immunpathologischer Vorgange fur kindliche
Lungenerkrankungen.
AU Weingartner L
SO ZEITSCHRIFT FUR ERKRANKUNGEN DER ATMUNGSORGANE, (1975 Jan) 142 (1) 18-29.
Journal code: XTN.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 197609
AB Under special conditions the lung develops reactions of hypersensitivity,
e.g. by the contact with antigens consisting of foreign proteins, organic
dusts or different pathogen organisms. It must be distinguished between
uncomplicated allergic and autoimmune diseases. The exact separation is
difficult, because transitions from one state to the other are possible.
The autoimmunisation is a very complicated phenomenon, where endogensou
cells are effective as auto-antigens and induce the development of
auto-antibodies. From the pathological-anatomical point of view thate are
no typical structural changes in the lung, which define a disease as a
special autoimmune disease. But the prevalence of round cells in inflamed
tissue, the appearance of granuloma with epithelial cells point to
immunological phenomenons. Examples for allergic diseases are: "Asthma
bronchiale, pigeon- ***breeder*** disease, mite-allergy, farmer's lung,
drug-induced allergy", and for autoimmune diseases: "Lupus erythematosus,
rheumatoid ***arthritis*** , polyarteritis nodosa, idiopathic
pulmonary hemosiderosis, idiopathic pulmonary fibrosis." The drug-therapy
consists of corticoids and immune-suppressive drugs.

=> file medline embase biosis inpadoc caplus

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		5.66	5.81

FILE 'MEDLINE' ENTERED AT 13:57:45 ON 25 JUL 2000

FILE 'EMBASE' ENTERED AT 13:57:45 ON 25 JUL 2000

FILE 'BIOSIS' ENTERED AT 13:57:45 ON 25 JUL 2000

FILE 'INPADOC' ENTERED AT 13:57:45 ON 25 JUL 2000

FILE 'CAPLUS' ENTERED AT 13:57:45 ON 25 JUL 2000

=> d his

(FILE 'HOME' ENTERED AT 13:51:53 ON 25 JUL 2000)

FILE 'MEDLINE' ENTERED AT 13:52:00 ON 25 JUL 2000
L1 16359 S BREEDING/AB,BI
L2 139 S L1 AND BALB?/AB,BI
L3 5 S L2 AND TRAIT#/AB,BI
L4 35308 S RHEUMATOID ARTHRITIS/AB,BI
L5 9 S L4 AND BREED?/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 13:57:45 ON 25
JUL 2000

=> s l5

'AB' IS NOT A VALID FIELD CODE
L6 34 L5

=> dup rem l6

PROCESSING COMPLETED FOR L6
L7 21 DUP REM L6 (13 DUPLICATES REMOVED)

=> s l7 and breeding/ab,bi

'AB' IS NOT A VALID FIELD CODE
L8 7 L7 AND BREEDING/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 7 MEDLINE
AN 97376834 MEDLINE
DN 97376834
TI High affinity rheumatoid factor transgenic B cells are eliminated in
normal mice.
AU Wang H; Shlomchik M J
CS Department of Laboratory Medicine, Yale University School of Medicine, New
Haven, CT 06520, USA.
NC P01 AI/ AR36529 (NIAID)
SO JOURNAL OF IMMUNOLOGY, (1997 Aug 1) 159 (3) 1125-34.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199710
EW 19971003
AB Although systemic autoimmune diseases can be accompanied by multiple
autoantibodies, certain specificities are dominant. Presumably, these
specificities and their cognate Ags have properties that make them
particularly amenable to autoimmune induction. Rheumatoid factors (RFs)
are a dominant class of autoantibodies in ***rheumatoid*** ***arthritis*** and certain other autoimmune syndromes. To study the
regulation of RFs in normal and autoimmune animals, we previously created
a RF Ig transgenic model based on an RF isolated from an autoimmune
MRL/lpr mouse. Using this model, called AM14, we were surprised to find
that normal mice do not regulate disease-related RF B cells. This raised
the question of whether RFs in general are not susceptible to tolerance
induction, perhaps due to the unique properties of serum IgG and its FcRs.
Alternatively, RFs can be tolerized, and the disease-related RFs are below
the affinity threshold for such tolerance. To distinguish these
possibilities, we generated a second RF transgenic model with the same
specificity but much higher affinity than AM14. We found that, in contrast
to AM14, high affinity RF B cells are subject to central tolerance,
showing that there is not an absolute defect in RF B cell tolerance, but,
rather, that RF B cell tolerance is affinity dependent even in normal
animals. This is also the first model in which a disease-related
specificity has been shown clearly to delete in a system in which
Ag-positive and negative mice can be produced and compared.

L8 ANSWER 2 OF 7 MEDLINE
AN 95142883 MEDLINE
DN 95142883
TI The viable motheaten (mev) mouse--a new model for arthritis.
AU Kovarik J; Kuntz L; Ryffel B; Borel J F
CS Immunology Department, Sandoz Pharma Ltd, Basel, Switzerland.
SO JOURNAL OF AUTOIMMUNITY, (1994 Oct) 7 (5) 575-88.
Journal code: ADL. ISSN: 0896-8411.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199505
AB Homozygous mev mice are first identified at the age of 3-4 days by focal
depigmentation of the skin, followed by patchy absence of hair and by
necrotic lesions on paws, tail and ears. Of particular interest are the
inflammatory reactions in the paws of these animals which consist mainly
of polymorphonuclear and mononuclear cell infiltration in the subcutaneous
tissue extending to the periosteum and joint, resulting in focal
destructive arthritis and osteomylitis. These lesions are to some extent
reminiscent of an acute form of rheumatoid-like arthritis. Since mev mice
are sterile, a limited number of symptomatic offspring can be obtained by
cross- ***breeding*** their heterozygous siblings which are
phenotypically not distinguishable from mice lacking this mutation. In
order to produce a sufficient number of diseased animals for performing
pharmacological studies, we have established a model by transferring this
disease in lethally irradiated, 8- to 10-week-old syngeneic mice which
were grafted with mev spleen cells. Such reconstituted recipients develop
first inflammatory symptoms of the paws 2 to 3 weeks after cell transfer.
The arthritic inflammation finally affects all paws and toes by 30 to 50
days. This procedure increased the number of mev-like mice expressing
arthritis, allowing assessment of the effects of standard reference drugs
used in the therapy of ***rheumatoid*** ***arthritis*** (RA). The
immunosuppressants cyclosporin and rapamycin and the steroid dexamethasone
at therapeutic concentrations exert a strong inhibitory effect on the
development of arthritis in this novel model. In contrast, the
non-steroidal anti-inflammatory drug phenylbutazone shows only a moderate
effect. These results indicate the particular sensitivity of this model
for efficacy of potentially new therapeutic but non-cytostatic compounds
for clinical use.

L8 ANSWER 3 OF 7 MEDLINE
AN 91224865 MEDLINE
DN 91224865
TI Juvenile-onset polyarthritis syndrome in Akitas.
AU Dougherty S A; Center S A; Shaw E E; Erb H A
CS Department of Clinical Science, New York State College of Veterinary
Medicine, Cornell University, Ithaca 14853-6401..
SO JOURNAL OF THE AMERICAN VETERINARY MEDICAL ASSOCIATION, (1991 Mar 1) 198
(5) 849-56.
Journal code: HAV. ISSN: 0003-1488.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199108
AB Two young Akitas were examined because of manifestation of a
juvenile-onset form of polyarthritis. A search of medical records at the
New York State College of Veterinary Medicine found 6 more similarly
affected Akitas. The clinical manifestations were marked by cyclic febrile
illness and signs of profound joint-related pain. Two dogs had concurrent
aseptic meningitis. The syndrome resembles juvenile ***rheumatoid***
arthritis in human beings, although it shares features with
systemic lupus erythematosus. Pedigree analysis of affected Akitas
supported a heritable component to the syndrome. Treatment with
immunosuppressive drugs was effective in 2 dogs that achieved

complete
remission, and in 2 dogs that achieved only partial remission. Classification of this syndrome is difficult and may represent an "overlap" syndrome commonly described in human beings.

L8 ANSWER 4 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 2000216142 EMBASE
TI Genetic control of arthritis in rats.
AU Holmdahl R.; Vingsbo-Lundberg C.; Nordquist N.; Olofsson P.; Sundvall M.;
Saxne T.; Pettersson U.
CS R. Holmdahl, Medical Inflammation Research, CMB, Lund University, Box 94,
S-221 00 Lund, Sweden. rikard.holmdahl@inflam.lu.se
SO Journal of Experimental Animal Science, (2000) 41/1-2 (7-13).
Refs: 23
ISSN: 0939-8600 CODEN: JEXSEU
CY Germany
DT Journal; Conference Article
FS 022 Human Genetics
LA English
SL English
AB This study was specifically designed to analyse the genetic control of the
chronic disease course for the development of arthritis. Arthritis models
with a chronic erosive arthritis are collagen induced arthritis induced
with homologous collagen in oil but also arthritis induced with certain
non-immunogenic adjuvants such as pristane and avridine. In the presently
described experiment we have used pristane induced arthritis. A single
injection of 150 .mu.l pristane induces severe chronic arthritis in DA
rats. The disease mimics ***rheumatoid*** ***arthritis*** in many
aspects such as the chronic disease course, an erosive inflammation of
peripheral joints, symmetric involvement of the joints and the development
of rheumatoid factors. To determine the genetic contribution we have used
a number of inbred, recombinant inbred and congenic strains as well as
specifically designed segregating crosses. An influence by the MHC region
(designated Pia1 locus) on the chronic disease course was determined
through the uses of MHC congenic LEW strains in which the RT1-f haplo-type
conferred highest susceptibility. To map genes outside of MHC we used an
F2 cross between the highly susceptible DA and the resistant E3 strains.
Loci exclusively associated with different phenotypes of the disease could
be identified. .cntdot. Arthritis onset (Pia2 and Pia3). .cntdot. Severity
and joint erosions (Pia4). .cntdot. Chronicity (Pia5 and Pia6) and Pia1
(determined from MHC congenic strains). These findings demonstrates that a
chronic self-perpetuative disease, mimicking ***rheumatoid*** ***arthritis*** , is controlled by different set of genes exclusively
linked to different phases of the disease course such as arthritis onset,
joint erosions, severity and chronicity.

L8 ANSWER 5 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 80054040 EMBASE
DN 1980054040
TI Early rheumatoid-like joint lesions in rabbits injected with foreign serum
or milk proteins. III. Influence of concomitant IgE-like antibodies and of
the ***breed*** of rabbit.
AU Oldham G.; Coombs R.R.A.
CS Div. Immunol., Dept. Pathol., Univ. Cambridge, United Kingdom
SO International Archives of Allergy and Applied Immunology, (1980) 61/1
(81-90).
CODEN: IAAAAM
CY Switzerland
DT Journal
FS 037 Drug Literature Index
031 Arthritis and Rheumatism
026 Immunology, Serology and Transplantation
LA English
AB The presence of circulating IgE-like antibody was found not to enhance the
induction of joint lesions, of moderate or greater intensity, by
intravenous injection of bovine serum, but did make mild joint lesions
more frequent. There was a positive correlation between increased white
cell effusion into the joint fluid and joint lesions of moderate or
greater intensity. Different ***breeds*** of rabbit were shown to
produce different incidences of lesions suggesting a genetic influence on
the development of rheumatoid-like joint lesions. The Old English
breed was found to be particularly sensitive.

L8 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:161442 BIOSIS
DN PREV199800161442
TI Acquired inhibitor to factor VIII: C in non hemophilia (acquired hemophilia). Clinico-biological study and management in nine patients.
AU Liozon, Eric (1); Delaire, Laurent; Turlure, Pascal; Jaccard, Arnaud;
Loustaud-Ratti, Veronique; Remenieras, Liliane; Julia, Annie; Gaillard,
Solange; Bordessoule, Dominique; Vidal, Elisabeth
CS (1) Serv. Med. Interne A., CHRU Dupuytren, 2 rue Martin-Luther-King, 87042
Limoges France
SO Annales de Medecine Interne, (Nov., 1997) Vol. 148, No. 7, pp. 477-490.
ISSN: 0003-410X.
DT Article
LA French
AB Study designs: To describe retrospectively the experience of the Internal
Medicine and Clinical Hematology Departments of a University Hospital on
adult acquired hemophilia (AH) caused by autoantibody against factor VIII
coagulant (f.VIII:C) activity. Diagnosis, clinical datas, associated
diseases, treatment and final outcome are described and compared to the
published literature. Material and methods. All cases admitted in both
departments since 1989 were enrolled in the study. Clotting analyses
comprised clotting times (activated partial thromboplastin time,
prothrombin and thrombine times), measurements of f.VIII:C level,
antifactor VIII detection and measurement by the Bethesda method assay.
Search for an etiologic factor could not be standardized. All patients
were followed until cure, sustained improvement, or death. Results: From
1989 to 1996. All was diagnosed in nine adult patients. Mean age was 76 +-
24.6 years (range: 65-89) and sex ratio male to female was 2. Eight
bleeding episodes occurred in seven patients, resulting consistently in
severe hemorrhagic anemia and leading to hemodynamic failure in two, while
two others remained asymptomatic for prolonged periods. The initial levels
of f.VIII:C ranged from less than 1% to 20%, and the titers of inhibitors
ranged from 0.5 to 100 Bethesda units. An underlying disease, to which the
appearance of their inhibitor could be related, either concomitantly or up
to 1 year later, was found in four cases including (one case each):
rheumatoid ***arthritis*** , lupus erythematosus with
antiphospholipid syndrome, followed by non-Hodgkin malignant lymphoma,
relapsing carcinoma and, biliary tract surgery. Six acute bleeding
episodes necessitated symptomatic measures, based on activated prothrombin
complex concentrates in four instances, with a good response in all

cases.
Preparation to minor surgical operations was achieved in two asymptomatic
subjects by either highly purified factor VIII concentrates infusion or
intravenous 1-desamino-8-D-arginine vasopressin, with a good control of
local hemostasis in each case. Three received intravenous immunoglobulins,
which resulted in success in one, failure in one and, questionable
response in the latter. Immunosuppression, mainly with corticosteroids,
cyclophosphamide, or both, was given to seven, resulting in disappearance
of inhibitor in rive (delay to cure ranged from 2 weeks to 10 months),
improvement in one, and failure in one (in this latter case, cure was
eventually achieved with the anti-Hodgkin disease MOPP chemotherapy).
After a 27-month mean follow-up, six patients experienced a sustained
complete response and one a sustained partial response to
immuno-suppression, two untreated patients remained asymptomatic, two died
later from malignancy (carcinoma and myelodysplastic syndrome).
Conclusion. - AH usually presents as a severe or even a life-threatening
disease, necessitating prompt and thorough symptomatic measures directed
at the cessation of ***breeding*** and prevention of their relapse. In
our experience, no death was attributable to AH or its treatment.
Immunosuppression is useful in selected cases, but must be carefully
discussed, since it can be highly toxic, especially in the elderly. Given
the possibility of a delayed onset of some etiologic factors, a prolonged
surveillance of each case of idiopathic AH is mandatory.

L8 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1993:455916 BIOSIS
DN PREV199396100816
TI Spontaneous production of Epstein-Barr virus by B lymphoblastoid cell
lines obtained from patients with Sjogren's syndrome: Possible involvement
of a novel strain of Epstein-Barr virus in disease pathogenesis.
AU Tateishi, Mutsuto; Saito, Ichiro; Yamamoto, Kohtaro; Miyasaka, Nobuyuki
(1)
CS (1) Dep. Virol. Immunol., Div. Immunol. Dis., Med. Res. Inst., Tokyo Med.
Dent. Univ., 1-5-45, Yushima, Bunkyo-ku, Tokyo Japan
SO Arthritis & Rheumatism, (1993) Vol. 36, No. 6, pp. 827-835.
ISSN: 0004-3591.
DT Article
LA English
AB Objective: To investigate the involvement of Epstein-Barr virus (EBV) in
the pathogenesis of Sjogren's syndrome (SS) and to examine whether the
spontaneous production of EBV is unique to SS B cell lines. Methods: B
cell lines were established from peripheral blood mononuclear cells (PBMC)
of patients with systemic lupus erythematosus, ***rheumatoid*** ***arthritis*** , and SS. The cord blood immortalization assay, flow
cytometric analysis, and polymerase chain reaction (PCR) were used to
detect EBV production by B cell lines. Results: SS B cell lines produced
EBV at a higher frequency, and in significantly larger amounts, than did
other B cell lines. However, no correlation with the amount of EBV DNA in
the genome of B cell lines was found. PCR analysis revealed that EBV with
a B95-8-like U2 region was dominant in SS B cell lines. Conclusion:
Spontaneous, massive production of EBV by B cell lines is unique to SS,and
may contribute to the polyclonal B cell activation seen in this disease.

=> s arthritis and model/ab,bi

'AB' IS NOT A VALID FIELD CODE
L9 12601 ARTHRITIS AND MODEL/AB,BI

=> s l9 and (mice or mouse)/ab,bi

'AB' IS NOT A VALID FIELD CODE
L10 3695 L9 AND (MICE OR MOUSE)/AB,BI

=> s l10 and progeny/ab,bi

'AB' IS NOT A VALID FIELD CODE
L11 20 L10 AND PROGENY/AB,BI

=> dup rem l11

PROCESSING COMPLETED FOR L11
L12 9 DUP REM L11 (11 DUPLICATES REMOVED)

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L12 ANSWER 1 OF 9 MEDLINE DUPLICATE 1
AN 2000139432 MEDLINE
DN 20139432
TI An integrated genetic linkage map with 1,137 markers constructed from five
F2 crosses of autoimmune disease-prone and -resistant inbred rat strains.
AU Dracheva S V; Remmers E F; Chen S; Chang L; Gulko P S; Kawahito Y; Longman
R E; Wang J; Du Y; Shepard J; Ge L; Joe B; Kotake S; Salstrom J L; Furuya
T; Hoffman J; Cannon G W; Griffiths M M; Wilder R L
CS The Inflammatory Joint Diseases Section, National Institute of Arthritis
and Musculoskeletal and Skin Diseases, Bethesda, Maryland 20892, USA.
SO GENOMICS, (2000 Jan 15) 63 (2) 202-26.
Journal code: GEN. ISSN: 0888-7543.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200006
EW 20000604
AB The rat (Rattus norvegicus) is an important experimental ***model***
for many human diseases including ***arthritis*** , diabetes, and other
autoimmune and chronic inflammatory diseases. The rat genetic linkage map,
however, is less well developed than those of ***mouse*** and human.
Integrated rat genetic linkage maps have been previously reported by
Pravenec et al. (1996, Mamm. Genome 7: 117-127) (500 markers mapped in one
cross), Bihoreau et al. (1997, Genome Res. 7: 434-440) (767 markers mapped
in three crosses), Wei et al. (1998, Mamm. Genome 9: 1002-1007) (562
markers mapped in two crosses), Brown et al. (1998, Mamm. Genome 9:
521-530) (678 markers mapped in four crosses), and Nordquist et al. (1999,
Rat Genome 5: 15-20) (330 markers mapped in two crosses). The densest
linkage map combined with a radiation hybrid map, reported by Steen et al.
(1999, Genome Res. 9: AP1-AP8), includes 4736 markers mapped in two
crosses. Here, we present an integrated linkage map with 1137 markers. We
have constructed this map by genotyping F2 ***progeny*** of five
crosses: F344/NHsd x LEW/NHsd (673 markers), DA/Bkl x F344/NHsd (531
markers), BN/SsN x LEW/N (714 markers), DA/Bkl x

BN/SsNHsd (194 markers),
and DA/Bkl x ACI/SegHsd (245 markers). These inbred rat strains vary in
susceptibility/resistance to multiple autoimmune diseases and are used
extensively for many types of investigation. The integrated map includes
360 loci mapped in three or more crosses. The map contains 196 new SSLP
markers developed by our group, as well as many SSLP markers developed by
other groups. Two hundred forty genes are incorporated in the map. This
integrated map should allow comparison of rat genetic maps from different
groups and thereby facilitate genetic studies of rat autoimmune and
related disease models. Copyright 2000 Academic Press.

L12 ANSWER 2 OF 9 MEDLINE DUPLICATE 2
AN 2000081743 MEDLINE
DN 20081743
TI Identification of multiple loci linked to inflammation and autoantibody
production by a genome scan of a murine ***model*** of rheumatoid
arthritis .
AU Otto J M; Cs-Szabo G; Gallagher J; Velins S; Mikecz K; Buzas E I; Enders J
T; Li Y; Olsen B R; Glant T T
CS Department of Biochemistry, Rush University at Rush-Presbyterian-St.
Luke's Medical Center, Chicago, Illinois 60612, USA.
NC AR-40310 (NIAMS)
AR-45652 (NIAMS)
SO ARTHRITIS AND RHEUMATISM, (1999 Dec) 42 (12) 2524-31.
Journal code: 90M. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200004
EW 20000401
AB OBJECTIVE: Proteoglycan-induced ***arthritis*** (PGIA) is a murine
model of rheumatoid ***arthritis*** (RA), both in terms of its
pathology and its genetics. PGIA can only be induced in susceptible murine
strains and their F2 ***progeny*** . As with RA, the genetics are
complex, containing both major histocompatibility complex (MHC)-related
and non-MHC-related components. Our goal was to identify the underlying
non-MHC-related loci that confer PGIA susceptibility.
METHODS: We used 106
polymorphic markers to perform simple sequence-length polymorphism
analysis on F2 hybrids of susceptible (BALB/c) and nonsusceptible (DBA/2)
strains of ***mice*** . Because both strains of ***mice*** share
the H2d haplotype, this cross permits identification and analysis of
non-MHC-related genes. RESULTS: We identified a total of 12 separate
quantitative trait loci (QTL) associated with PGIA, which we have named
Pgia1 through Pgia12. QTLs associated with the inflammatory symptoms of
PGIA were linked to chromosomes 7, 9, 15 (2 separate loci), 16, and 19.
QTLs associated with autoantibody production were identified on
chromosomes 1, 2, 7, 8, 10, 11, 16, and 18. QTLs on chromosomes 7 and 16
showed linkage to both inflammation and autoantibody production,
suggesting a shared regulatory component in ***arthritis*** induction.
The first inflammation QTL on chromosome 15 and the autoantibody QTL on
chromosome 7 originate from the DBA/2 background, which indicates that as
in RA, susceptibility genes can originate from heterogeneous backgrounds.
CONCLUSION: These data demonstrate the complexity of PGIA, where QTLs may
be involved in multiple traits or even originate from a genetic background
previously determined to be resistant.

L12 ANSWER 3 OF 9 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 1999246754 EMBASE
TI Identification of a new quantitative trait locus on Chromosome 7 controlling disease severity of collagen-induced ***arthritis*** in
rats.
AU Dracheva S.V.; Remmers E.F.; Gulko P.S.; Kawahito Y.; Longman R.E.; Reese
V.R.; Cannon G.W.; Griffiths M.M.; Wilder R.L.
CS R.L. Wilder, Inflammatory Joint Diseases Section, National Institutes Of
Health, Bldg. 10, 10 Center Drive, Bethesda, MD 20892, United States.
wilderr@arb.niams.nih.gov
SO Immunogenetics, (1999) 49/9 (787-791).
Refs: 36
ISSN: 0093-7711 CODEN: IMNGBK
CY Germany
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
022 Human Genetics
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LA English
SL English
AB Autoimmune diseases, such as rheumatoid ***arthritis*** , Crohn's
disease, and multiple sclerosis, are regulated by multiple genes. Major
histocompatibility complex (MHC) genes have the strongest effects, but
non-MHC genes also contribute to disease susceptibility/severity. In this
paper, we describe a new non-MHC quantitative trait locus, Cia8, on rat
Chromosome (Chr) 7 that controls collagen-induced ***arthritis***
severity in F2 ***progeny*** of DA and F314 inbred rats, and present
an updated localization of Cia4 on the same chromosome. We also describe
the location of ***mouse*** and human genes, orthologous to the genes
in the genomic intervals containing Cia4 and Cia8, and provide evidence
that the segment of rat Chr 7 containing Cia4 and Cia8 is homologous to
segments of ***mouse*** Chr 10 and 15 and human Chr 8, 12, and 19.

L12 ANSWER 4 OF 9 MEDLINE DUPLICATE 3
AN 1998451500 MEDLINE
DN 98451500
TI Localization of quantitative trait loci regulating adjuvant-induced ***arthritis*** in rats: evidence for genetic factors common to multiple
autoimmune diseases.
AU Kawahito Y; Cannon G W; Gulko P S; Remmers E F; Longman R E; Reese V R;
Wang J; Griffiths M M; Wilder R L
CS The Inflammatory Joint Diseases Section, Arthritis and Rheumatism Branch,
National Institute of Arthritis and Musculoskeletal and Skin Diseases,
Bethesda, MD 20892-1820, USA.
SO JOURNAL OF IMMUNOLOGY, (1998 Oct 15) 161 (8) 4411-9.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199901
AB Adjuvant-induced ***arthritis*** (AIA) in rats is a widely used
autoimmune experimental ***model*** with many features similar to
rheumatoid ***arthritis*** (RA). To identify potential genetic
regulatory mechanisms in RA, we conducted genome-wide linkage analysis in

F2 ***progeny*** of ***arthritis*** -susceptible Dark Agouti (DA)
and relatively resistant Fischer 344 (F344) inbred rats. We compared the
data with our previously reported investigation of collagen-induced
arthritis (CIA), which was expanded in the follow-up study
reported in this work. We found two quantitative trait loci (QTLs) in
common, i.e., Aia1/Cia1 on chromosome 20, which includes the MHC, and
Aia3/Cia3 on chromosome 4. We also identified a second unique QTL in AIA,
Aia2, on chromosome 4. Interestingly, the QTL region on chromosome 4
(Aia3/Cia3), like the MHC, appears to be involved in several other
autoimmune diseases in rats, including insulin-dependent diabetes,
thyroiditis, and experimental autoimmune uveitis. Moreover, an analysis of
conserved synteny among rats, ***mice*** , and humans suggested that
Aia2 and Aia3/Cia3, like Aia1/Cia1, contain candidate genes for several
autoimmune/inflammatory diseases in ***mice*** and humans, including
diabetes, systemic lupus erythematosus, inflammatory bowel disease,
asthma/atopy, multiple sclerosis, and RA. The rat models appear to provide
a powerful complementary approach to identify and characterize candidate
genes that may contribute to autoimmune diseases in several species.

L12 ANSWER 5 OF 9 MEDLINE DUPLICATE 4
AN 97426595 MEDLINE
DN 97426595
TI Mapping of ***mouse*** obesity genes: A generic approach to a complex
trait.
AU Fisler J S; Warden C H
CS Department of Medicine, Division of Cardiology, University of California,
Los Angeles, CA 90095, USA.
SO JOURNAL OF NUTRITION, (1997 Sep) 127 (9) 1909S-1916S. Ref: 78
Journal code: JEV. ISSN: 0022-3166.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199712
EW 19971204
AB Identification of genes underlying any complex trait such as obesity is an
important and difficult problem in genetics. Traditional candidate gene
approaches cannot be relied on to identify all of the genes influencing a
complex trait, and positional cloning is very laborious. With the advent
of new tools and methods, however, comprehensive approaches to the
identification of any genes underlying complex traits are now available.
Quantitative trait locus (QTL) mapping is a general technique to map
Mendelian factors influencing complex traits. The QTL approach involves
the crossing of two strains that differ in the trait of interest to
produce F2 or back-cross ***progeny*** , individually phenotyping and
genotyping each ***progeny*** , and statistically associating the typed
markers and the phenotype. QTL mapping has been used in the last 4 years
to map genes for a wide variety of traits, including body weight and
growth, obesity, atherosclerosis and susceptibility to cancer in the
mouse , and hypertension, hyperactivity and ***arthritis*** in
the rat. QTL mapping has also been used to map genes in pigs, poultry,
cows, fish and plants. Once a trait has been located in a chromosomal
subregion, identifying the underlying gene remains a significant problem.
A monogenic ***model*** must be developed, isolating one gene
influencing a trait from other genes affecting the same phenotype. Then
the positional candidate strategy, which relies on a combination of
mapping to a chromosomal subregion followed by a survey of the interval to
see if attractive candidates reside there, becomes practical.

L12 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2000 ACS
AN 1997:595664 CAPLUS
DN 127:276143
TI Mapping of ***mouse*** obesity genes: a genetic approach to a complex
trait
AU Fisler, Janis S.; Warden, Craig H.
CS Dep. of Medicine, Division of Cardiology, University of California, Los
Angeles, CA, 90095, USA
SO J. Nutr. (1997), 127(9), 1909S-1916S
CODEN: JONUAI; ISSN: 0022-3166
PB American Society for Nutritional Sciences
DT Journal; General Review
LA English
AB A review with 78 refs. Identification of genes underlying any complex
trait such as obesity is an important and difficult problem in genetics.
Traditional candidate gene approaches cannot be relied on to identify all
of the genes influencing a complex trait, and positional cloning is very
laborious. With the advent of new tools and methods, however, comprehensive
approaches to the identification of any genes underlying complex traits are now
available. Quant. trait locus (QTL) mapping is a general technique to map
Mendelian factors influencing complex traits.
The QTL approach involves the crossing of two strains that differ in the
trait of interest to produce F2 or back-cross ***progeny*** ,
individually phenotyping and genotyping each ***progeny*** , and
statistically assocg. the typed markers and the phenotype. QTL mapping
has been used in the last 4 yr to map genes for a wide variety of traits,
including body wt. and growth, obesity, atherosclerosis, and
susceptibility to cancer in the ***mouse*** , and hypertension,
hyperactivity, and ***arthritis*** in the rat. QTL mapping has also
been used to map genes in pigs, poultry, cows, fish, and plants. Once a
trait has been located in a chromosomal subregion, identifying the
underlying gene remains a significant problem. A monogenic ***model***
must be developed, isolating one gene influencing a trait from other genes
affecting the same phenotype. Then the positional candidate strategy,
which relies on a combination of mapping to a chromosomal subregion
followed by a survey of the interval to see if attractive candidates
reside there, becomes practical.

L12 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:483636 BIOSIS
DN PREV199497496636
TI Collagen-induced ***arthritis*** and TCRs in SWR and B10.Q
mice expressing an F-alpha-kappa transgene.
AU Griffiths, Marie M. (1); Nabozny, Gerald H.; Hanson, Julie; Harper, D.
Scott; McCall, Shawna; Moder, Kevin G.; Cannon, Grant W.; Luthra,
Harvinder S.; David, Chella S.
CS (1) Div. Rheumatol., Dep. Med., Univ. Utah Med. Sch., 50 North Medical
Dr., Salt Lake City, UT 84132 USA
SO Journal of Immunology, (1994) Vol. 153, No. 6, pp. 2758-2768.
ISSN: 0022-1767.
DT Article

LA English
AB B10.E-alpha-k transgenic ***mice*** were mated with H2-E-B10.Q and
SWR ***mice*** . F-1 and F-1 times parental strain backcross ***progeny*** were tested for ***arthritis*** and autoimmune
reactivity to ***mouse*** type II collagen (MII) after immunization
with bovine, chick, deer, or human type 11 collagen. The results were
correlated with the H-2 haplotype (b/q vs q/q) and the TCR VP profile of
peripheral blood T cells in each ***mouse*** . Hybrid ***progeny***
expressed TCR profiles different from either parent because of the TCR VP
genomic deletions of SWR ***mice*** (VP'), the wild-type TCR allele of
C57Bl/10 (B10) ***mice*** (V-beta-b), and the intrathymic negative
selection processes resulting from cell surface expression of
E-alpha-k-A-beta-q or E-beta-b-E-alpha-k, together with the integrated
retroviral genes Mtv-9 originating in B10 ***mice*** and
Mtv-7(Mls-1-a) from SWR ***mice*** . (B10.E-alpha-k times SWR)F-1
mice developed higher IgG anti-MII Ab titers, but much milder
arthritis than (B10.E times B10.Q)F-1 ***mice*** . Expression
of Ek did not change the level of IgG anti-MII Ab nor the degree of
susceptibility to collagen-induced ***arthritis*** (CIA) in the
H-2-q/q and H-2-b/q ***progeny*** of (B10.E-alpha-k times B10.Q)F-1 x
B10.Q matings, indicating that the Mtv-9-reactive, TCR V-beta-5+, and
V-beta-11+ T cells are not critical to CIA. Among bovine type II
collagen-immunized (B10.E-alpha-k times SWR)F-1 times SWR backcross
mice : 1) ***arthritis*** severity is associated with the
presence of V-beta-b (p ltoreq 0.01) and expression of E-alpha-k (p ltoreq
0.05), but not with the MHC haplotype (b/q vs q/q); 2) regression analysis
showed a significant association (R = 0.99) between IgG anti-MII Ab titers
and the level of Mtv-7-reactive V-beta-6+ T cells that was detectable in
the IgG I, but not the IgG2a subclass. The data prompt the speculation
that Mtv-7-reactive V-beta-6+ (or V-beta-7+) T cells in (B10.E-alpha-k X
SWR)F-1 x SWR ***mice*** express Th2-type properties, and thus
contribute to the combination of mild ***arthritis*** but high
anti-MII Ab titers that characterize ***mice*** of SWR heritage.

L12 ANSWER 8 OF 9 MEDLINE DUPLICATE 5
AN 91310083 MEDLINE
DN 91310083
TI The role of C5 and T-cell receptor Vb genes in susceptibility to collagen-induced ***arthritis*** [see comments].
CM Comment in: Immunogenetics 1992;35(1):69-70
Comment in: Immunogenetics 1992;35(1):71-2; discussion 73-4
AU Spinella D G; Jeffers J R; Reife R A; Stuart J M
CS Veterans Administration Medical Center, Memphis, TN 38104..
NC AR39166 (NIAMS)
SO IMMUNOGENETICS, (1991) 34 (1) 23-7.
Journal code: GI4. ISSN: 0093-7711.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199110
AB Collagen-induced ***arthritis*** (CIA) is a rodent ***arthritis***
model in which immunization with heterologous type II collagen
induces an inflammatory polyarthritis. Susceptibility to the disease is
mediated by major histocompatibility complex (MHC) genes as well as genes
at other loci. Previous studies of the SWR/J ***mouse*** strain, which
is resistant to CIA despite bearing the susceptible H-2q haplotype, have
suggested that this resistance is the result of a deletion of T-cell
receptor (Tcr) Vb gene segments which is carried by this strain. Other
studies have implicated a deficiency in complement component C5 as the
cause for the resistance. In order to assess the relative importance of
these two genes in susceptibility to CIA, and to provide an estimate of
the number of independent genes involved in the disease, we analyzed 196
F2 ***progeny*** of a (DBA/1 x SWR/J) cross for ***arthritis***
susceptibility, and expression of both C5 and Tcr genes. Thirty of the F2
progeny developed ***arthritis*** . All of the arthritic
mice had at least one copy of the wild-type C5 allele, while the
Tcr-Vb haplotypes were distributed in Mendelian fashion. These results
demonstrate that C5 sufficiency is an absolute requirement for CIA, but
that Tcr-Vb genes located within the SWR deletion have little influence.
Genetic analysis of the incidence rate suggests that there is polygenic
control of susceptibility to CIA and that in addition to H-2, 5-6 other
independent loci (including C5) may be involved.

L12 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1991:431916 BIOSIS
DN BA92:88081
TI THE ROLE OF C5 AND T-CELL RECEPTOR VB GENES IN SUSCEPTIBILITY TO
COLLAGEN-INDUCED ***ARTHRITIS*** .
AU SPINELLA D G; JEFFERS J R; REIFE R A; STUART J M
CS VA MED. CENT., 1030 JEFFERSON AVE., MEMPHIS, TENN. 38104, USA.
SO IMMUNOGENETICS, (1991) 34 (1), 22-27.
CODEN: IMNGBK. ISSN: 0093-7711.
FS BA; OLD
LA English
AB Collagen-induced ***arthritis*** (CIA) is a rodent ***arthritis***
model in which immunization with heterologous type II collagen
induces an inflammatory polyarthritis. Susceptibility to the disease is
mediated by major histocompatibility complex (MHC) genes as well as genes
at other loci. Previous studies of the SWR/J ***mouse*** strain, which
is resistant to CIA despite bearing the susceptible H-2q haplotype, have
suggested that this resistance is the result of a deletion of T-cell
receptor (Tcr) Vb gene segments which is carried by this strain. Other
studies have implicated a deficiency in complement component C5 as the
cause for the resistance. In order to assess the relative importance of
these two genes in susceptibility to CIA, and to provide an estimate of
the number of independent genes involved in the disease, we analyzed 196
F2 ***progeny*** of a (DBA/1 .times. SWR/J) cross for
arthritis susceptibility, and expression of both C5 and Tcr genes.
Thirty of the F2 ***progeny*** developed ***arthritis*** . All of
the arthritic ***mice*** had at least one copy of the wild-type C5
allele, while the Tcr-Vb haplotypes were distributed in Mendelian fashion.
These results demonstrate that C5 sufficiency is an absolute requirement
for CIA, but that Tcr-Vb genes located within the SWR deletion have little
influence. Genetic analysis of the incidence rate suggests that there is
polygenic control of susceptibility to CIA and that in addition to H-2,

5-6 other independent loci (including C5) may be involved.

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FILE 'MEDLINE' ENTERED AT 14:04:55 ON 25 JUL 2000

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=> s rheumatoid arthritis and screening/ab,bi

62441 RHEUMATOID
84571 ARTHRITIS
35308 RHEUMATOID ARTHRITIS
(RHEUMATOID(W)ARTHRITIS)
135856 SCREENING/BI
5361026 AB/FA
77715 SCREENING/AB
(SCREENING/BI (L) AB/FA)
135856 SCREENING/BI
L13 272 RHEUMATOID ARTHRITIS AND SCREENING/AB,BI

=> s l13 and therap?/ab,bi

1932856 THERAP?/BI
5361026 AB/FA
459694 THERAP?/AB
(THERAP?/BI (L) AB/FA)
1932856 THERAP?/BI
L14 76 L13 AND THERAP?/AB,BI

=> s l14 and model/ab,bi

336283 MODEL/BI
5361026 AB/FA
298097 MODEL/AB
(MODEL/BI (L) AB/FA)
336283 MODEL/BI
L15 9 L14 AND MODEL/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L15 ANSWER 1 OF 9 MEDLINE
AN 1999255070 MEDLINE
DN 99255070
TI Anticomplement activity of triterpenes from Crataeva nurvala stem bark in
adjuvant arthritis in rats.
AU Geetha T; Varalakshmi P
CS Department of Medical Biochemistry, Dr. A.L. Mudaliar Post Graduate
Institute of Basic Medical Sciences, University of Madras, Chennai, India.
SO GENERAL PHARMACOLOGY, (1999 Apr) 32 (4) 495-7.
Journal code: FLK. ISSN: 0306-3623.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
EW 19990901
AB Adjuvant arthritis is widely used as an experimental ***model*** for
rheumatoid ***arthritis*** and inflammation. It is useful in
the evaluation of anti-inflammatory drugs. Lupeol is a naturally occuring
triterpene isolated from Crataeva nurvala stem bark, and its ester lupeol
linoleate was synthesized. The effects of lupeol and lupeol linoleate on
the development of complement in adjuvant arthritis in rats were studied
and compared with those of indomethacin. The effect of lupeol linoleate in
reducing the foot-pad thickness and complement activity in arthritic rats
was even greater than that of unesterified lupeol and indomethacin.
Because complement is highly involved in inflammation, the results suggest
that the anti-inflammatory activity of triterpenes may be due to their
anticomplementary activity.

L15 ANSWER 2 OF 9 MEDLINE
AN 97349900 MEDLINE
DN 97349900
TI Pharmacological profile of the novel potent antirheumatic
4-(2',4'-difluorobiphenyl-4-yl)-2-methyl-4-oxobutanoic acid.
AU Panajotova V; Anderova E; Jandera A; Kuchar M
CS VUFB, a.s. (Research Institute for Pharmacy and Biochemistry), Prague,
Czech Republic.
SO ARZNEIMITTEL-FORSCHUNG, (1997 May) 47 (5) 648-52.
Journal code: 91U. ISSN: 0004-4172.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
EW 19971003
AB On the basis of basic ***screening*** for novel, more potent
antiarthritics VUFB-16066
(4-(2',4'-difluorobiphenyl-4-yl)-2-methyl-4-
oxobutanoic acid, CAS 112344-S2-2) was chosen as a compound with
pronounced anti-inflammatory and immunomodulatory effects, with good
gastric tolerance and relatively low toxicity. VUFB-16066 is a dual
cyclooxygenase and 5-lipoxygenase inhibitor, and it suppresses
alloantigen-driven cellular immune response and phagocytosis of stimulated
peritoneal cells. VUFB-16066 exhibits prolonged pharmacological activity
connected with its major metabolite having a very long half-life. In the
model of adjuvant arthritis VUFB-16066 improves most of disease
symptoms including immunopathological disturbances, which indicates
possible disease-modifying activity of the drug. The beneficial
antiarthritic effect of VUFB-16066 has been also confirmed in patients
with ***rheumatoid*** ***arthritis*** .

L15 ANSWER 3 OF 9 MEDLINE
AN 95149828 MEDLINE
DN 95149828
TI Antirheumatic drug profiles evaluated in the adjuvant arthritis of rats by
multiparameter analysis.
AU Theisen-Popp P; Muller-Peddinghaus R
CS Bayer A. G. Wuppertal, Germany..
SO AGENTS AND ACTIONS, (1994 Aug) 42 (1-2) 50-5.
Journal code: 2XZ. ISSN: 0065-4299.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

EM 199505
AB Freund's adjuvant arthritis (FAA) in susceptible rats (male, Lewis strain)
is a well-established experimental ***model*** of ***rheumatoid***
arthritis to evaluate inherent drug properties, i.e.
anti-inflammatory and/or immunosuppressive/immunomodulatory properties
which are only ascertained by combining multiple parameter analysis. We
employed a synoptic multiparametric evaluation system for the multifaceted
FAA, a so-called "spider scheme", to facilitate a more rapid and easier
comparison of qualitative and quantitative drug properties by visual
display than that achieved by mere tabulation of the data. The spider
scheme comprised six well-established parameters to evaluate the FAA
disease (primary and secondary hind paw swelling, arthritic index which
included macroscopic alterations of non-injected paws, nose, ears and
tail, body weight changes and relative organ weights of thymus and
spleen). By calculation of an index as a percent change in comparison to
control and untreated diseased animals, the degree of improvement or
impairment of the FAA by a tested compound could easily be entered into
the spider scheme. The FAA parameter spider scheme clearly differentiated
the most beneficial immunomodulatory properties of cyclosporin A from
those of the immunosuppressive agents dexamethasone and cyclophosphamide
as well as from the mere anti-inflammatory cyclooxygenase inhibitors.
Among this latter class of non-steroidal anti-inflammatory compounds, a
similar profile was demonstrated for indometacin and diclofenac, as well
as for tenidap, which is claimed to have cytokine-modulating properties,
as reflected by the reduction of acute-phase proteins in patients with
rheumatoid ***arthritis*** . Yet, in this FAA ***model*** ,
with tenidap, no additional qualitative drug properties could be
discerned.(ABSTRACT TRUNCATED AT 250 WORDS)

L15 ANSWER 4 OF 9 MEDLINE
AN 94244233 MEDLINE
DN 94244233
TI A clinical and biochemical assessment of methotrexate in ***rheumatoid*** ***arthritis*** .
AU Tait T J; Le Gallez P; Astbury C; Bird H A
CS Clinical Pharmacology Unit (Rheumatism Research) Royal Bath Hospital,
North Yorkshire, United Kingdom..
SO CLINICAL RHEUMATOLOGY, (1994 Mar) 13 (1) 75-9.
Journal code: DI6. ISSN: 0770-3198.
CY Belgium
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199408
AB Low-dose methotrexate has gained widespread acceptance as a second-line
agent in ***rheumatoid*** ***arthritis*** (RA). The Leeds Human
Model ***Screening*** System (LHMSS) is a validated
screening mechanism allowing the rapid evaluation of compounds for
their potential as anti-rheumatic agents, the results of which have been
confirmed in longer term studies. We have evaluated methotrexate in
patients with RA using the LHMSS at a maintenance dose of 10mg/week.
Significant change occurred in four out of eleven variables over a 24-week
period ($p < 0.01$). This degree of change is greater than that seen with
nonsteroidal anti-inflammatory agents but less than with other recognised
second-line agents such as D-penicillamine, suggesting that methotrexate
may have less potential as a second-line agent than D-penicillamine.

L15 ANSWER 5 OF 9 MEDLINE
AN 92336640 MEDLINE
DN 92336640
TI [Celiac disease in adults: clinical aspects--role of endoscopy].
La maladie coeliaque de l'adulte: aspects cliniques--role de l'endoscopie.
AU Mainguet P; Degrez T; Jouret A; Haot J
CS U.C.L., Cliniques Universitaires Saint-Luc, Bruxelles, Belgique..
SO ACTA GASTROENTEROLOGICA BELGICA, (1992 Mar-Apr) 55 (2) 181-9. Ref: 65
Journal code: 0NY. ISSN: 0001-5644.
CY Belgium
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA French
EM 199210
AB Adult coeliac disease has a broad clinical spectrum and remains undetected
for years. Among subclinical deficiency states, attributable to coeliac
enteropathy, combined iron and folic acid malabsorption is predominant. An
unexplained recurrent iron anaemia is an indication for small intestinal
biopsy. Gastro-intestinal disorders are present in only 50% of the cases.
Coeliac disease is frequently associated with other major
histocompatibility complex (MMC)-linked diseases which are mediated by
immunological mechanisms: dermatitis herpetiformis, oral ulcerations, IgA
nephropathy, ***rheumatoid*** ***arthritis*** , sarcoidosis.
Dermatitis herpetiformis is a useful ***model*** for examination of
the spectrum of mucosal changes that typify gluten sensitivity and
subliminal lesions without villous atrophy. An increased interest is
devoted to the intra-epithelial T-lymphocyte population, not only in the
small intestine, but at the level of the stomach and the colon. A "rectal
challenge" test has been proposed for detecting gluten sensitivity in
coeliac patients. Such a test could be an original method of
screening , reducing so the need of small intestinal biopsy. The
preliminary results are to be confirmed. Until now, jejunoscopy remains
mandatory for the diagnosis and the survey of intestinal lesions related
to coeliac disease.

L15 ANSWER 6 OF 9 MEDLINE
AN 91295099 MEDLINE
DN 91295099
TI C-reactive protein as an index of disease activity. Comparison of tenidap,
cyclophosphamide and dexamethasone in rat adjuvant arthritis.
AU Otterness I G; Pazoles P P; Moore P F; Pepys M B
CS Pfizer Central Research Division, Department of Immunology and Infectious
Diseases, Groton, CT 06340..
SO JOURNAL OF RHEUMATOLOGY, (1991 Apr) 18 (4) 505-11.
Journal code: JWX. ISSN: 0315-162X.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199110
AB C-reactive protein (CRP) concentrations are a useful plasma protein
measure that correlate with disease severity and radiographic progression
in ***rheumatoid*** ***arthritis*** (RA). We compared 3 drugs with
different mechanisms, i.e., tenidap, dexamethasone and cyclophosphamide,
on both CRP levels and soft tissue swelling in the rat adjuvant arthritis

model . CRP rose from a normal concentration of approximately 400
micrograms/ml during the first phase of adjuvant arthritis to approximately 1200 micrograms/ml (primary response), then fell to approximately 900 micrograms/ml and rose again as the disease became
systemic during the secondary response to approximately 1400 micrograms/ml. When treatment was administered prophylactically, tenidap
and dexamethasone suppressed both the primary and secondary CRP and
swelling responses. Cyclophosphamide was without effect in the primary
response, but inhibited both swelling and CRP in the secondary response.
When ***therapeutic*** treatment was begun after secondary disease was
established, only tenidap and dexamethasone inhibited CRP and swelling.
Both dexamethasone and cyclophosphamide decreased lymphocyte numbers
during treatment whereas lymphocyte numbers were elevated during tenidap
treatment, suggesting a different mechanism of action for tenidap. CRP
levels were more closely linked to the rate of change of paw swelling
(disease progression) than to paw volume.

L15 ANSWER 7 OF 9 MEDLINE
AN 91153918 MEDLINE
DN 91153918
TI Murine delayed-type hypersensitivity granuloma: an improved ***model***
for the identification and evaluation of different classes of anti-arthritic drugs.
AU Dunn C J; Galinet L A; Gibbons A J; Shields S K
CS Department of Hypersensitivity Disease Research, Upjohn Company,
Kalamazoo, Michigan 49001..
SO INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (1990) 12 (8) 899-904.
Journal code: GRI. ISSN: 0192-0561.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199106
AB The present study examined the effects of five different classes of
anti-inflammatory/immunoregulatory drugs using a mouse ***model*** of
mBSA-induced delayed-type hypersensitivity granuloma (DTH GRA) to measure
immune-mediated chronic inflammatory tissue formation. The compounds were
administered orally daily following induction of DTH GRA (days 0 to 4);
granulomata were quantitated gravimetrically on day 5. NSAIDs, with the
exception of flurbiprofen, showed little activity in comparison with the
steroids dexamethasone (1-3 mg/kg/day, orally) and prednisolone (3-10
mg/kg/day, orally), which caused significant suppression of DTH GRA tissue
(65-76% and 26-68%, respectively). The "immunoregulatory" compounds
levamisole and D(-)penicillamine were inactive, whereas cyclophosphamide
(5-50 mg/kg/day, orally) reduced the response by 24-83%. The "interferon
alpha-inducers" Tilorone, U-54,461, and U-56,499 were also potent
inhibitors of the DTH GRA response; U-54,462, a weak interferon
alpha-inducer, was inactive. Cyclosporin A (50-100 mg/kg/day, orally)
suppressed DTH GRA most effectively when administered on days 3 and 4 (66%
and 97%) of the five-day granuloma response (treatment was ineffective
when given on days 1 and 2). We conclude that the DTH GRA response
described above may be useful for evaluating different types of unique
therapeutic agents that are effective in the treatment of chronic
immuno-inflammatory disease such as ***rheumatoid*** ***arthritis***

L15 ANSWER 8 OF 9 MEDLINE
AN 86115177 MEDLINE
DN 86115177
TI Studies on the effect of low dose methotrexate on rat adjuvant arthritis.
AU Welles W L; Silkworth J; Oronsky A L; Kerwar S S; Galivan J
NC CA 25933 (NCI)
SO JOURNAL OF RHEUMATOLOGY, (1985 Oct) 12 (5) 904-6.
Journal code: JWX. ISSN: 0315-162X.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198605
AB Adjuvant arthritis in rats was induced by the intradermal administration
of Freund's complete adjuvant. When these immunized rats were treated
orally with low doses of methotrexate (150-600 micrograms/kg/week) a
statistically significant suppression of paw inflammation was observed.
This low dose of methotrexate was comparable to that used in the treatment
of human ***rheumatoid*** ***arthritis*** (RA). Our results are
the first demonstration of the efficacy of low dose methotrexate in an
animal ***model*** of human RA.

L15 ANSWER 9 OF 9 MEDLINE
AN 75205164 MEDLINE
DN 75205164
TI Chemistry and pharmacology of naproxen.
AU Dorfman R I
SO ARZNEIMITTEL-FORSCHUNG, (1975 Feb) 25 (2A) 278-81.
Journal code: 91U. ISSN: 0004-4172.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197511
AB The need for a nonsteroidal anti-inflammatory agent effective in
rheumatoid ***arthritis*** , osteoarthritis, gout, ankylosing
spondylitis and related diseases with reduced side effects when compared
to existing drugs led us to develop naproxen: d-2-(6'-methoxy-2'-naphthyl)-
propionic acid. This new agent is a highly effective anti-inflammatory,
analgetic, and antipyretic agent in the rodent administered orally. In a
rat paw edema test for anti-inflammatory activity naproxen was 55 times
more active than aspirin. Analgetic activity was assessed by three
different assay procedures. In the mouse phenylquinone writhing test
naproxen was 7 times as effective as aspirin. In the rat yeast-induced paw
edema and the rat carrageenin paw edema analgetic assays the test compound
was 10 and 20 times more effective than aspirin, respectively. A
yeast-induced pyresis ***model*** in the rat indicated that naproxen
was 22 times more potent than the standard aspirin. The relative potency
of naproxen to phenylbutazone and indometacin is presented.

=> d his

(FILE 'HOME' ENTERED AT 13:51:53 ON 25 JUL 2000)

FILE 'MEDLINE' ENTERED AT 13:52:00 ON 25 JUL 2000
L1 16359 S BREEDING/AB,BI
L2 139 S L1 AND BALB?/AB,BI
L3 5 S L2 AND TRAIT#/AB,BI
L4 35308 S RHEUMATOID ARTHRITIS/AB,BI
L5 9 S L4 AND BREED?/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 13:57:45 ON 25 JUL 2000
L6 34 S L5
L7 21 DUP REM L6 (13 DUPLICATES REMOVED)
L8 7 S L7 AND BREEDING/AB,BI
L9 12601 S ARTHRITIS AND MODEL/AB,BI
L10 3695 S L9 AND (MICE OR MOUSE)/AB,BI
L11 20 S L10 AND PROGENY/AB,BI
L12 9 DUP REM L11 (11 DUPLICATES REMOVED)

FILE 'MEDLINE' ENTERED AT 14:04:55 ON 25 JUL 2000
L13 272 S RHEUMATOID ARTHRITIS AND SCREENING/AB,BI
L14 76 S L13 AND THERAP?/AB,BI
L15 9 S L14 AND MODEL/AB,BI

=> s balb?/ab,bi

69950 BALB?/BI
5361026 AB/FA
22759 BALB?/AB
(BALB?/BI (L) AB/FA)
69950 BALB?/BI
L16 69950 BALB?/AB,BI

=> s l16 and arthritis/ab,bi

84571 ARTHRITIS/BI
5361026 AB/FA
37193 ARTHRITIS/AB
(ARTHRITIS/BI (L) AB/FA)
84571 ARTHRITIS/BI
L17 368 L16 AND ARTHRITIS/AB,BI

=> s l17 and model/ab,bi

336283 MODEL/BI
5361026 AB/FA
298097 MODEL/AB
(MODEL/BI (L) AB/FA)
336283 MODEL/BI
L18 79 L17 AND MODEL/AB,BI

=> s l18 and rheumatoid/ab,bi

62441 RHEUMATOID/BI
5361026 AB/FA
27717 RHEUMATOID/AB
(RHEUMATOID/BI (L) AB/FA)
62441 RHEUMATOID/BI
L19 43 L18 AND RHEUMATOID/AB,BI

=> s l19 and screen?/ab,bi

170430 SCREEN?/BI
5361026 AB/FA
112946 SCREEN?/AB
(SCREEN?/BI (L) AB/FA)
170430 SCREEN?/BI
L20 0 L19 AND SCREEN?/AB,BI

=> s l18 and screen?/ab,bi

170430 SCREEN?/BI
5361026 AB/FA
112946 SCREEN?/AB
(SCREEN?/BI (L) AB/FA)
170430 SCREEN?/BI
L21 1 L18 AND SCREEN?/AB,BI

=> d bib ab

L21 ANSWER 1 OF 1 MEDLINE
AN 1998283922 MEDLINE
DN 98283922
TI The preclinical pharmacological profile of the potent and selective leukotriene B4 antagonist CP-195543.
AU Showell H J; Conklyn M J; Alpert R; Hingorani G P; Wright K F; Smith M A; Stam E; Salter E D; Scampoli D N; Meltzer S; Reiter L A; Koch K; Piscopio A D; Cortina S R; Lopez-Anaya A; Pettipher E R; Milici A J; Griffiths R J
CS Department of Cancer, Immunology and Infectious Diseases, Pfizer Inc, Groton, Connecticut, USA.
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1998 Jun) 285 (3) 946-54. Journal code: JP3. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
EW 19980902
AB CP-195543 [(+)-2-(3-benzyl-4-hydroxy-chroman-7-yl)-4-trifluoromethyl-benzoic acid] is a structurally novel, selective and potent leukotriene B4 (LTB4) receptor antagonist. In vitro CP-195543 inhibited [3H]LTB4 binding to high-affinity LTB4 receptors on human neutrophils (HN) and murine spleen membranes with IC50 values of 6.8 nM (Ki = 4.9 nM) and 37.0 nM (Ki = 26.9 nM), respectively. CP-195543 inhibited human and mouse neutrophil chemotaxis mediated by LTB4 with IC50 values of 2.4 nM and 7.5 nM, respectively. Evidence of noncompetitive antagonist effects on the HN high-affinity LTB4 receptor was obtained by Scatchard analysis of [3H]LTB4 binding to and chemotaxis of HN to LTB4. Scatchard analyses of [3H]LTB4 binding to low-affinity receptors on HN indicated that CP-195543 acted as a competitive antagonist at this receptor, and inhibition of LTB4-mediated CD11b up-regulation on HN was inhibited competitively by CP-195543 (pA2 = 7.66). In whole blood, CP-195543 also blocked CD11b up-regulation on HN (pA2 = 7.12) and murine neutrophils (pA2 = 7.06) with a similar potency. LTB4-mediated CD11b up-regulation on human monocytes and eosinophils in whole blood were inhibited by CP-195543 with IC50 values of 270 nM and 420 nM, respectively. CP-195543 at 10 microM failed to inhibit HN chemotaxis and CD11b up-regulation mediated through alternative (i.e., complement fragment 5a, interleukin-8, platelet-activating factor) G-protein-coupled chemotactic factor receptors. In vivo, after oral administration, CP-195543 blocked LTB4-mediated neutrophil infiltration in guinea pig and murine skin with ED50 values of 0.1 mg/kg and 2.8 mg/kg p.o., respectively. When administered in osmotic pumps, CP-195543 reduced the clinical symptoms and attendant weight loss in an IL-1-exacerbated murine ***model*** of collagen-induced ***arthritis*** with half-maximal effects associated with plasma drug levels of 0.4 to 0.5 microg/ml. Collectively these data provide evidence of the in vitro potency and in vivo efficacy of a novel LTB4 antagonist and support its clinical evaluation in a variety of inflammatory diseases in man.

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FILE 'MEDLINE' ENTERED AT 13:52:00 ON 25 JUL 2000
L1 16359 S BREEDING/AB,BI
L2 139 S L1 AND BALB?/AB,BI
L3 5 S L2 AND TRAIT#/AB,BI
L4 35308 S RHEUMATOID ARTHRITIS/AB,BI
L5 9 S L4 AND BREED?/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 13:57:45 ON 25
JUL 2000
L6 34 S L5
L7 21 DUP REM L6 (13 DUPLICATES REMOVED)
L8 7 S L7 AND BREEDING/AB,BI
L9 12601 S ARTHRITIS AND MODEL/AB,BI
L10 3695 S L9 AND (MICE OR MOUSE)/AB,BI
L11 20 S L10 AND PROGENY/AB,BI
L12 9 DUP REM L11 (11 DUPLICATES REMOVED)

FILE 'MEDLINE' ENTERED AT 14:04:55 ON 25 JUL 2000
L13 272 S RHEUMATOID ARTHRITIS AND SCREENING/AB,BI
L14 76 S L13 AND THERAP?/AB,BI
L15 9 S L14 AND MODEL/AB,BI
L16 69950 S BALB?/AB,BI
L17 368 S L16 AND ARTHRITIS/AB,BI
L18 79 S L17 AND MODEL/AB,BI
L19 43 S L18 AND RHEUMATOID/AB,BI
L20 0 S L19 AND SCREEN?/AB,BI
L21 1 S L18 AND SCREEN?/AB,BI

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JUL 2000

=> s l21

'AB' IS NOT A VALID FIELD CODE
L22 1 L21

=> s l19

'AB' IS NOT A VALID FIELD CODE
L23 125 L19

=> s l23 and (drug# or therap?)/ab,bi

2 FILES SEARCHED...
'AB' IS NOT A VALID FIELD CODE
L24 44 L23 AND (DRUG# OR THERAP?)/AB,BI

=> dup rem l24

PROCESSING COMPLETED FOR L24
L25 36 DUP REM L24 (8 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 36 ANSWERS - CONTINUE? Y/(N):y

L25 ANSWER 1 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 2000204547 EMBASE
TI In vitro and in vivo inhibition of activation induced T cell apoptosis by
bucillamine.
AU Okazaki H.; Sato H.; Kamimura T.; Hirata D.; Iwamoto M.; Yoshio T.; Mimori
A.; Masuyama J.-I.; Kano S.; Minota S.
CS Dr. S. Minota, Div. of Rheumatol./Clin. Immunology, Department of
Medicine, Jichi Medical School, Minamikawachi-Machi, Tochigi-Ken 329-04,
Japan
SO Journal of Rheumatology, (2000) 27/6 (1358-1364).
Refs: 36
ISSN: 0315-162X CODEN: JRHUA
CY Canada
DT Journal; Article
FS 031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
AB Objective. To investigate the mechanism of autoimmune phenomena,
occasionally seen in patients with ***rheumatoid*** ***arthritis***
treated with bucillamine (BUC) and D-penicillamine (D-Pen), by evaluating
their effects on apoptosis of T cells induced by T cell receptor
activation or dexamethasone. Methods. In vitro apoptosis was induced in a
T cell hybridoma (SSP3.7) and a B cell line (WEHI 231) by activation of
respective receptors or dexamethasone, in the presence or absence of BUC
or D-Pen. In vivo apoptosis was induced in ***BALB*** /c mice by
staphylococcal enterotoxin B (SEB), with or without BUC or D-Pen, and
thymocytes were examined for it by FACS. Results. Stimulation with
anti-CD3 and dexamethasone induced apoptosis in 72% and 71% of SSP3.7
cells, respectively. However, only 16% of SSP3.7 cells became apoptotic by
anti-CD3 when BUC was added to the culture media. By contrast, 80% of
SSP3.7 cells became apoptotic when stimulated by dexamethasone, even in
the presence of BUC. BUC did not affect apoptosis of WEHI 231 cells
induced by anti-IgM. Although SA981 (a metabolite of BUC) inhibited
apoptosis of SSP3.7 cells induced by anti-CD3, D-Pen did not. BUC, SA981,
or D-Pen did not significantly influence the level of interleukin 2
secretion stimulated by anti-CD3. In contrast, both BUC and D-Pen
inhibited apoptosis of V.beta.8+ thymocytes induced in vivo by SEB
superantigen. Neither BUC nor D-Pen significantly changed the number of
CD4+CD8+ thymocytes in ***BALB*** /c mice injected with dexamethasone.
Conclusion. BUC decreased, while D-Pen did not, the apoptosis of T cells
stimulated by anti-CD3 in vitro, although they both inhibited the deletion
of immature thymocytes reactive with SEB in vivo. This may explain
autoimmune phenomena sometimes seen during the treatment of rheumatic
patients with these ***drugs*** .

L25 ANSWER 2 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 2000102718 EMBASE
TI A novel dual regulator of tumor necrosis factor-.alpha. and interleukin-10
protects mice from endotoxin-induced shock.
AU Fukuda T.; Sumichika H.; Murata M.; Hanano T.; Adachi K.; Hisadome M.
CS T. Fukuda, Research Laboratories, Yoshitomi Pharmaceutical Industries, 955
Koiwai, Yoshitomi-cho, Chikujo-gun, Fukuoka 871-8550, Japan
SO European Journal of Pharmacology, (17 Mar 2000) 391/3 (317-320).
Refs: 8
ISSN: 0014-2999 CODEN: EJPHAZ
PUI S 0014-2999(00)00096-0
CY Netherlands
DT Journal; Article
FS 029 Clinical Biochemistry
030 Pharmacology

037 ' Drug Literature Index
004 Microbiology
LA English
SL English
AB A pyrimidylpiperazine derivative,
N-[1-(4-{[4-(pyrimidin-2-yl)piperazin-1-
yl]methyl}phenyl)cyclopropyl]acetamide (Y-39041), is a dual cytokine
regulator of tumor necrosis factor (TNF)-.alpha. and interleukin-10
production. Lipopolysaccharide-induced TNF-.alpha. release in ***BALB***
/c mice was inhibited by the oral treatment with the compound at 10-100
mg/kg (about 80% suppression) while interleukin-10 release was augmented
(about 10-fold increase at 30 mg/kg). In addition, Y-39041 (30 mg/kg,
p.o.) completely protected mice from lipopolysaccharide-induced death by
the treatment before and after lipopolysaccharide injection. The finding
that Y-39041 suppresses TNF-.alpha. production and stimulates
interleukin-10 production at the same time provides new insights for the
treatment of septic shock, ***rheumatoid*** ***arthritis*** and
Crohn's diseases. Copyright (C) 2000 Elsevier Science B.V.

L25 ANSWER 3 OF 36 MEDLINE DUPLICATE 1
AN 1999226861 MEDLINE
DN 99226861
TI Modulation of hyaluronan receptor (CD44) function in vivo in a murine
model of ***rheumatoid*** ***arthritis*** .
AU Mikecz K; Dennis K; Shi M; Kim J H
CS Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois 60612, USA.
NC AR-44126 (NIAMS)
SO ARTHRITIS AND RHEUMATISM, (1999 Apr) 42 (4) 659-68.
Journal code: 90M. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199907
EW 19990702
AB OBJECTIVE: To determine how in vivo modulation of CD44 function by
antibodies influences disease severity in a murine ***model*** of
rheumatoid ***arthritis*** . METHODS: Mice with proteoglycan
(PG)-induced ***arthritis*** were subjected to systemic treatment with
3 different monoclonal antibodies against CD44. Joint swelling and serum
levels of hyaluronan (HA) and soluble CD44 (sCD44) were monitored.
Inflammatory leukocyte infiltration in the joints, cell surface CD44
expression, and leukocyte adhesion to HA were compared. The effects of
anti-CD44 treatment on the immune status of arthritic animals were also
determined. RESULTS: Antibody IRAWB14, which enhances HA binding,
aggravated the inflammatory symptoms, while KM201, which blocks ligand
binding, reduced the severity of ***arthritis*** . The most effective
suppression of inflammation was noted upon treatment with antibody IM7,
whose epitope lies outside the HA binding domain of CD44. Serum levels of
sCD44 increased, and HA levels decreased, in response to IM7. KM201 and
IM7 treatment reduced, but IRAWB14 treatment enhanced, the adhesion of
leukocytes to HA. However, these antibodies had little effect on
PG-specific immune responses. CONCLUSION: Each antibody acted in vivo by
virtue of its combined effects on CD44-HA binding and CD44 shedding. The
dramatic reduction in ***arthritis*** severity effected by IM7
treatment was associated with extensive shedding of cell surface CD44
molecules. Loss of CD44 appears to be a major factor in preventing CD44-
and HA-dependent cell-matrix interactions at the inflammatory site. Our
study indicates a critical role for CD44 in the pathology of joint
inflammation and reveals a unique mechanism of receptor down-regulation,
which can be used ***therapeutically*** .

L25 ANSWER 4 OF 36 MEDLINE
AN 2000075381 MEDLINE
DN 20075381
TI Functional definition of a B cell epitope, KGEQGEPGA, on C1q the
Fc-binding subunit of the first component of complement.
AU Trinder P K; Marker-Hermann E; Loos M; Maeurer M J
CS Institute of Medical Microbiology & Hygiene, Hochhaus am Augustusplatz,
Mainz, Germany.
SO SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1999 Dec) 50 (6) 635-41.
Journal code: UCW. ISSN: 0300-9475.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 200003
EW 20000303
AB A synthetic peptide representing the C1q epitope KGEQGEPGA has been shown
to suppress or delay the onset of CII-induced ***arthritis*** when
applied intravenously (i.v.) prior to an intradermal (i.d.) challenge, in
a mouse ***model*** ; the phenomenon being associated with the
development of immunoglobulin (Ig)M antibodies specific for the KGEQGEPGA
epitope. Here we show that this amino acid sequence provides an
immunodominant B cell epitope that is recognised by autoantibodies present
in the sera of patients with chronic inflammatory diseases such as
systemic lupus erythematosus (SLE) and ***rheumatoid*** ***arthritis*** , two diseases associated with an immune response to C1q.
The peptide's ability to produce peptide specific IgM when applied i.v. in
both normal and athymic mice but not in mice exhibiting the x-linked
B-cell associated Bruton's tyrosine kinase defect permits classification
of the KGEQGEPGA peptide as a T-cell independent antigen type-2 (TI-2).
IgM monoclonal antibodies raised against the peptide are able to
functionally block activation of the complement cascade by C1q, via a
mechanism that inhibits the C4 consumption. Antibodies to this
immunodominant epitope may therefore modulate inflammatory processes by
interfering with the activation of the classical pathway of the complement.

L25 ANSWER 5 OF 36 MEDLINE
AN 1999132578 MEDLINE
DN 99132578
TI Methotrexate specifically modulates cytokine production by T cells and
macrophages in murine collagen-induced ***arthritis*** (CIA): a
mechanism for methotrexate-mediated immunosuppression.
AU Neurath M F; Hildner K; Becker C; Schlaak J F; Barbulescu K; Germann T;
Schmitt E; Schirmacher P; Haralambous S; Pasparakis M; Meyer Zum
Buschenfelde K H; Kollias G; Marker-Hermann E
CS Laboratory of Immunology, I Medical Clinic, University of Mainz, Germany.
SO CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1999 Jan) 115 (1) 42-55.
Journal code: DD7. ISSN: 0009-9104.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199904

EW 19990403
AB Immunosuppressive ***therapy*** with methotrexate (MTX) has been
established as effective treatment for patients with ***rheumatoid***
arthritis . To analyse the ***therapeutic*** potential and
mechanisms of action of MTX, we determined serum cytokine levels and
cytokine production by splenic T cells and macrophages in untreated and
MTX-treated mice. Furthermore, we assessed the role of MTX in a murine
model of experimental ***arthritis*** induced by collagen type
II (CIA). MTX reduced spontaneous and IL-15-induced tumour necrosis factor
(TNF) production by splenic T cells but not by macrophages from healthy
mice in vitro in a dose-dependent manner. In contrast, interferon-gamma
(IFN-gamma) production was less strikingly reduced and IL-4 production was
virtually unaffected. In addition, treatment of healthy mice with MTX in
vivo led to reduced TNF serum levels and diminished TNF production by
splenic T cells and macrophages. Intraperitoneal administration of MTX
prior to the onset of ***arthritis*** completely prevented clinical
and pathological signs of CIA. This was associated with a striking
reduction of TNF production by spleen cells from MTX-treated mice. The
role of TNF in MTX-mediated effects on cytokine production was further
underlined by the finding that MTX effects on IFN-gamma production were
augmented in TNF-transgenic mice but abrogated in mice in which the
TNF-alpha gene had been inactivated by homologous recombination. Thus, MTX
specifically modulates spontaneous and IL-15-induced TNF-alpha production
in mice and prevents experimental murine CIA. These data suggest that TNF
production by T cells is an important target of MTX and may serve as a
basis to understand and further analyse MTX-mediated mechanisms of
immunosuppression in patients with RA.

L25 ANSWER 6 OF 36 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:407141 BIOSIS
DN PREV199800407141
TI Antitumor effect of gold as revealed by growth suppression of cultured
cancer cells.
AU Koide, Tatsurou; Kojima, Takashi; Kamei, Hideo (1)
CS (1) 2 Suemori-dori, Chikusa, Nagoya 464-0821 Japan
SO Cancer Biotherapy & Radiopharmaceuticals, (June, 1998) Vol. 13, No. 3, pp.
189-192.
ISSN: 1084-9785.
DT Article
LA English
AB Gold agents have been widely used for the treatment of ***rheumatoid***
arthritis . We studied the growth inhibiting effect of such an
agent on malignant cells in vitro. HCT-15, AGS cells derived from a human
malignancy, and Meth/A cells from a malignant lymphoma of ***Balb*** /C
mice were cultured separately with gold agent at concentrations of 2
mug/ml. Four days after the cultures had been incubated in a 5% CO2
incubator at 37degreeC, cell counts were made; and significance of
differences was analyzed by Student's t test. Additionally, HCT- 1 5 cells
were cultured with gold for two days, and then the cells were analyzed by
flow cytometry. The growth of HCT-15, AGS, and Meth/A cells was suppressed
by gold. Fifty percent suppression was observed at a concentration between
50 mug/ml and 10 mug/ml for HCT-15 cells, between 125 mug/ml and 50 mug/ml
for AGS cells, and between 125 mug/ml and 50 mug/ml for Meth/A cells.
Fifty percent suppression of HCT-15 cell growth by cisplatinum was found
between 50 mug/ml and 10 mug/ml. Flow cytometric findings showed a
significant rise in the tetraploid peak, a mild rise in the resion between
diploid and tetraploid peaks, and an increase in cells with a ploidy
greater than four. These data suggest that gold blocks the S phase, G2 to
M phase, and M phase as well. To observe the cytotoxicity of gold, each of
10 of 4 week-old ***Balb*** /C mice was injected s. c. at a dose of 10
mg/kg or 2 mg/kg every other day for a total of 3 injections, or was
administered the gold at 30 mg/kg/day p.o. injected s.c. one time into
each of 10 mice, and 60% of the animals died within 10 days after the
injection.

L25 ANSWER 7 OF 36 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:323640 BIOSIS
DN PREV199800323640
TI The role of platelet activating factor and other lipid mediators in
inflammatory angiogenesis.
AU Jackson, Jeffrey R. (1); Bolognese, Brian; Mangar, Clare A.; Hubbard,
Walter C.; Marshall, Lisa A.; Winkler, James D.
CS (1) Dep. Immunopharmacol., UW2532, SmithKline Beecham Pharmaceuticals, 709
Swedeland Rd., King of Prussia, PA 19406 USA
SO Biochimica et Biophysica Acta, (May 20, 1998) Vol. 1392, No. 1, pp.
145-152.
ISSN: 0006-3002.
DT Article
LA English
AB Chronic inflammatory diseases are often accompanied by intense
angiogenesis. A ***model*** of inflammatory angiogenesis is the murine
air pouch granuloma which has a hyperangiogenic component. Proinflammatory
lipid mediator generation is also a hallmark of chronic inflammation and
the role of endogenous production of these mediators in angiogenesis is
not known. The 14 kDa phospholipase A2 (PLA2) deacylates phospholipid,
liberating arachidonic acid, which is used for leukotriene production, and
lysophospholipid, which can drive the production of platelet-activating
factor (PAF). Therefore, SB 203347, an inhibitor of the 14 kDa PLA2,
zileuton, an inhibitor of 5-lipoxygenase, and Ro 24-4736 a PAF receptor
antagonist were evaluated for their effects in the murine air pouch
granuloma. SB 203347 reduced both LTB4 and PAF, but not PGD2 levels
measured in the day 6 granuloma. This correlated with a significant
reduction in angiogenesis. Zileuton reduced LTB4 levels as expected, but
did not significantly inhibit angiogenesis, whereas Ro 24-4736 potently
reduced angiogenesis. These data support the hypothesis that PAF, and to a
lesser extent leukotrienes contribute to the angiogenic phenotype in
chronic inflammation.

L25 ANSWER 8 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 2
AN 1999020861 EMBASE
TI Susceptibility of human synovial cells in four strains of SCID mice.
AU Abe C.; Yamada H.; Kikukawa T.; Ishii O.; Ichikawa Y.; Hioki K.; Endo S.
CS Prof. C. Abe, 5-15-3 Higashishinkoiwa, Tokyo 124-0023, Japan
SO International Journal of Immunotherapy, (1998) 14/3 (129-133).
Refs: 12
ISSN: 0255-9625 CODEN: IJIMET
CY Switzerland

DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LA English
SL English
AB Human synovial cells from patients with ***rheumatoid*** ***arthritis*** were transferred to four strains of severe combined immunodeficient (SCID) mice. C.B-17-SCID, ***BALB*** /cA-SCID, ***BALB*** /cA-bg-SCID (beige gene: low natural killer cell activity) and RAG2-deficient mice were studied. Synovial tissue-infiltrating cells were obtained from an explant culture of synovial tissues derived from patients with ***rheumatoid*** ***arthritis*** . Synovial tissue-infiltrating cells were injected into the right knee and dorsal side of foot joint of the animals at 6 weeks of age. Five weeks after the injection, a histopathological study was carried out under light microscope. The study revealed evidence that transplanted human cells made characteristic lesions in the mice, i.e., multiplication of synovial cells, proliferation of fibroblasts, fibrin exudation neovascularization, bone and cartilage replacement by connective tissue, and pannus formation. The most remarkable and characteristic lesions were observed in RAG2-deficient mice, then ***BALB*** /cA-bg-SCID, ***BALB*** /cA-SCID and C.B-17-SCID mice, respectively. A highly reproducible experimental animal ***model*** of ***arthritis*** was established by human synovial cells under in vivo transfer circumstances. It is possible that the human/RAG2 chimeric ***model*** is useful for studies on the pathogenesis of ***arthritis*** and the development or evaluation of ***therapeutic*** agents.

L25 ANSWER 9 OF 36 MEDLINE
AN 97263535 MEDLINE
DN 97263535
TI Experimental expression in mice and spontaneous expression in human SLE of polyomavirus T-antigen. A molecular basis for induction of antibodies to DNA and eukaryotic transcription factors.
AU Rekvig O P; Moens U; Sundsfjord A; Bredholt G; Osei A; Haaheim H; Traavik T; Arnesen E; Haga H J
CS Department of Immunology, University Hospital of Tromso, Norway..
olepr@fagmed.uit.no
SO JOURNAL OF CLINICAL INVESTIGATION, (1997 Apr 15) 99 (8) 2045-54.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199707
EW 19970703
AB We have previously demonstrated that experimental expression of the polyomavirus transcription factor T-antigen has the potential to induce anti-DNA antibodies in mice. Two sets of independent evidences are presented here that demonstrate a biological relevance for this ***model*** . First, we describe results demonstrating that mice inoculated with T-antigen-expressing plasmids produced antibodies, not only to T-antigen and DNA, but also to the DNA-binding eukaryotic transcription factors TATA-binding protein (TBP), and to the cAMP-response-element-binding protein (CREB). Secondly, we investigated whether polyomavirus reactivation occurs in SLE patients, and whether antibodies to T-antigen, DNA, and to TBP and CREB are linked to such events. Both within and among these SLE patients, frequent polyomavirus reactivations were observed that could not be explained by certain rearrangements of the noncoding control regions, nor by corticosteroid treatment. Linked to these events, antibodies to T-antigen, DNA, TBP, and CREB were detected, identical to what we observed in mice. Antibodies recognizing double-stranded DNA were confined to patients with frequent polyomavirus reactivations. The results described here indicate that cognate interaction of B cells recognizing DNA or DNA-associated proteins and T cells recognizing T antigen had taken place as a consequence of complex formation between T ag and DNA in vivo in the context of polyomavirus reactivations.

L25 ANSWER 10 OF 36 MEDLINE
AN 1998065302 MEDLINE
DN 98065302
TI Tranilast inhibits the proliferation, chemotaxis and tube formation of human microvascular endothelial cells in vitro and angiogenesis in vivo.
AU Isaji M; Miyata H; Ajisawa Y; Takehana Y; Yoshimura N
CS Discovery Research, R & D, Kissei Pharmaceutical Co., Ltd., Nagano-Pref., Japan.
SO BRITISH JOURNAL OF PHARMACOLOGY, (1997 Nov) 122 (6) 1061-6.
Journal code: B00. ISSN: 0007-1188.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
AB 1. First developed as an antiallergic ***drug*** , tranilast inhibits chemical mediator release from mast cells. In the present study, we examine the effects of tranilast on angiogenesis in vitro and in vivo and discuss the application of tranilast for angiogenic diseases. 2. Tranilast inhibited significantly the proliferation (IC50: 136 microM, 95% confidence limits: 134-137 microM) and vascular endothelium growth factor (VEGF)-induced chemotaxis (IC50: 135 microM, 95% confidence limits: 124-147 microM) of human dermal microvascular endothelial cells (HDMECs) at concentrations greater than 25 micrograms ml-1. No toxicity to HDMECs measuring by LDH release and no inhibitory effects on metalloproteinase (MMP)-2 and MMP-9 activity were observed even at 100 micrograms ml-1 (306 microM). 3. Tube formation of HDMECs cultured on the matrigel as an in vitro angiogenesis ***model*** was inhibited by tranilast in a concentration-dependent manner. The IC50 value and 95% confidence limits were 175 microM and 151-204 microM, respectively. 4. In vivo angiogenesis was induced in mice by the subcutaneous injection of matrigel containing 30 ng ml-1 VEGF and 64 micrograms ml-1 heparin. Tranilast was administered orally twice a day for 3 days. Tranilast dose-dependently suppressed angiogenesis in the matrigel and a significant change was observed at a dose of 300 mg kg-1. 5. These results indicate that tranilast is an angiogenesis inhibitor which may be beneficial for the improvement of angiogenic diseases such as proliferative diabetic retinopathy, age-related macular degeneration, tumour invasion and ***rheumatoid*** ***arthritis*** .

L25 ANSWER 11 OF 36 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:403517 BIOSIS
DN PREV199799709720
TI New nortriterpenoid isolated from anti- ***rheumatoid***

arthritic
plant, Tripterygium wilfordii, modulates tumor growth and neovascularization.
AU Ushiro, Shin; Ono, Mayumi; Nakayama, Juichiro; Fujiwara, Tadami; Komatsu,
Yasuhiro; Sugimachi, Keizo; Kuwano, Michihiko (1)
CS (1) Dep. Biochemistry, Kyushu Univ. Sch. Med., Maidashi, Fukuoka 812-82
Japan
SO International Journal of Cancer, (1997) Vol. 72, No. 4, pp. 657-663.
ISSN: 0020-7136.
DT Article
LA English
AB Preparations of Tripterygium wilfordii, "Thunder God vine", have been used
in China to treat ***rheumatoid*** ***arthritis*** .
Rheumatoid ***arthritis*** , as well as solid tumors, is
closely associated with neovascularization. Antiarthritic ***drugs***
therefore may modulate tumor growth as well as neovascularization. We
found that a compound purified from T. wilfordii, the nortriterpenoid,
demethylzeylasteral (TZ-93), inhibited the proliferation of vascular
endothelial cells approximately 30 times more effectively than it did for
the proliferation of human tumor cells. In in vitro assays using bovine
aortic endothelial cells, TZ-93 at non-toxic doses inhibited cell
migration, expression of urokinase-type plasminogen activator (uPA) mRNA
and uPA activity. Exogenous addition of uPA restored the inhibitory effect
of TZ-93 on cell migration. In dorsal air-sac assays in ***BALB*** /c
mice, the oral administration of 3 mg/kg/day TZ-93 for 5 days partially
inhibited, and 30 mg/kg/day almost completely abrogated, the development
of capillary networks induced by human hepatoblastoma cells. Similarly,
0.3 mg/kg/day TZ-93 partially inhibited, and 3 or 30 mg/kg/day almost
completely blocked, the growth of mouse B16-F10 melanoma cells in a tumor
implantation assay. The highest dose of TZ-93 significantly reduced the
growth of well-vascularized tumors with volumes of more than 500 mm-3.
TZ-93 treatment of tumor-bearing mice significantly decreased the density
of microvessels in the tumors. We conclude that TZ-93 may be useful in
treating highly vascularized and metastatic tumors as well as other
angiogenic diseases.

L25 ANSWER 12 OF 36 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:396766 BIOSIS
DN PREV199799695969
TI The influence of topical application of Oeparol (evening primrose oil) on
skin neovascular response induced in mice by leucocytes of
rheumatoid ***arthritis*** patients.
AU Sommer, Ewa; Skopinska-Rozewska, Ewa; Demkow, Urzula; Balan, Barbara;
Kleniewska, Danuta; Barcz, Ewa; Marczak, Maria
CS Instytut Gruzlicy Chorob Pluc, ul. Plocka 26, 01-138 Warszawa Poland
SO Reumatologia (Warsaw), (1997) Vol. 35, No. 2, pp. 166-170.
ISSN: 0034-6233.
DT Article
LA Polish
SL Polish; English
AB Aberrant neovascularisation occurs in several diseases such as psoriasis,
rheumatoid ***arthritis*** , and neoplasia, and plays in
important role in their pathogenesis. Antiangiogenic ***therapy***
seems to be a valuable addition to classical pharmacotherapy for diseases
dependent on uncontrolled neovascularisation. It is widely known that
plant substances may modulate functions of immune cells without several
side effects. In recent years there have been edited a lot of reports on
the beneficial effects of primrose extracts rich in unsaturated fatty
acids, and different mineral substances. The aim of our study was to
estimate the influence of primrose oil (Oeparol Agropharm) on angiogenic
activity of human leucocytes of 7 healthy blood donors, and leucocytes
with excess angiogenic activity from 5 ***rheumatoid***
arthritis patients. Cells were grafted intradermally to
immunosuppressed ***Balb*** /c mice. On the day of implantation and on
the following 2nd and 3rd day the primrose oil was applied on the sites of
injection. After 72 hours mice were sacrificed and new blood vessels were
counted. Primrose oil has decreased high angiogenic activity of leucocytes
of ***rheumatoid*** ***arthritis*** patients, and has had no
influence on healthy donors cells.

L25 ANSWER 13 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 97273376 EMBASE
DN 1997273376
TI TAK-603 selectively suppresses Th1-type cytokine production and inhibits
the progression of adjuvant ***arthritis*** .
AU Ohta Y.; Yamane M.; Sohda T.; Makino H.
CS Dr. Y. Ohta, Pharmaceutical Research Lab. I, Takeda Chemical Industries
Ltd., 17-85, Jusohonmachi, 2-Chome, Yodogawa-ku, Osaka 532, Japan
SO Immunology, (1997) 92/1 (75-83).
Refs: 47
ISSN: 0019-2805 CODEN: IMMUAM
CY United Kingdom
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
AB We have shown that TAK-603, a new anti-rheumatic ***drug*** , is more
effective in animal models in which cellular immunity plays a central
role. Here, we studied the effect of the ***drug*** on Th1 cytokines,
which are dominantly produced in this type of immune reaction, in an in
vitro system and an in vivo ***model*** . We established Th1- and
Th2-dominant T-cell lines, and studied the effect of TAK-603 on their
cytokine production. Th1 cell lines were ***BALB*** /c mouse
allo-reactive T cells and C57BL mouse mite antigen- reactive T cells, and
the Th2 cell line was ***BALB*** /c mouse ovalbumin-reactive T cells.
TAK-603 suppressed the production of Th1 cytokines [interferon-.gamma.
(IFN-.gamma.) and interleukin-2 (IL-2)] and riot that of Th2 cytokines
(IL-4, IL- 5) in these cell lines. Furthermore, selective suppression of
Th1 cytokine production was also observed in the T-cell clones obtained
from the ovalbumin-reactive T-cell line. To investigate the effect on
cytokine production in animal models of ***arthritis*** ; we analysed
the expression of cytokine messenger RNA using reverse
transcription-polymerase chain reaction in adjuvant ***arthritis***
rats, Th1-dominant cytokine production was observed both in the arthritic
joint and the spleen, and the time-course paralleled the progression of
arthritis . On the other hand, in type-II collagen- induced
arthritis , in which TAK-603 has little effect, Th1-dominant
cytokine production was not observed and Th2 cytokines were shown to be

more important. The adjuvant ***arthritis*** rats treated with TAK-603
(6.25 mg/kg/day, per os) showed significantly lower cytokine mRNA
expression both locally and systemically. These data suggest that TAK-603
selectively suppresses Th1 cytokine production, which is consistent with
its effect on cellular immunity in animal models.

L25 ANSWER 14 OF 36 MEDLINE
AN 96164593 MEDLINE
DN 96164593
TI TNF/IL-1-inducible protein TSG-6 potentiates plasmin inhibition by
inter-alpha-inhibitor and exerts a strong anti-inflammatory effect in vivo.
AU Wisniewski H G; Hua J C; Poppers D M; Naime D; Vilcek J; Cronstein B N
CS Department of Microbiology, Kaplan Cancer Center, New York University
Medical Center, NY 10016, USA.
NC R35 CA49731 (NCI)
AR/AI 41911 (NIAMS)
AR11949 (NIAMS)
+
SO JOURNAL OF IMMUNOLOGY, (1996 Feb 15) 156 (4) 1609-15.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199605
AB TNF-stimulated gene 6 (tsg6), encoding a 35-kDa secretory glycoprotein
(TSG-6), is induced in fibroblasts, chondrocytes, synovial cells, and
mononuclear cells by the proinflammatory cytokines TNF-alpha and IL-1, or
by LPS. Large amounts of TSG-6 protein were found in synovial fluids of
patients with ***rheumatoid*** ***arthritis*** . TSG-6 protein
forms a stable complex with components of the serine protease inhibitor,
inter-alpha-inhibitor (I alpha I). In this work, we show that TSG-6
potentiates the inhibitory effect of I alpha I on the protease activity of
plasmin. The plasmin/plasminogen activator system is important in the
protease network associated with inflammation. To test the hypothesis that
through their cooperative inhibitory effect on plasmin TSG-6 and I alpha I
can modulate the protease network and thus inhibit inflammation, we
examined the effect of TSG-6 on experimentally induced inflammation. Human
recombinant TSG-6 protein showed a potent anti-inflammatory activity in
the murine air pouch ***model*** of carrageenan- or IL-1-induced acute
inflammation. The inhibitory effect of locally administered TSG-6 on the
IL-1-induced cellular infiltration was comparable with that of systemic
dexamethasone treatment. Two mutant TSG-6 proteins with single amino acid
substitutions close to the N terminus showed a complete or partial loss of
anti-inflammatory activity. The anti-inflammatory effect of the
TNF/IL-1-inducible TSG-6 protein, along with its ability to inhibit
protease action through interaction with I alpha I, suggests that TSG-6
production during inflammation is part of a negative feedback loop
operating through the protease network.

L25 ANSWER 15 OF 36 MEDLINE
AN 96193613 MEDLINE
DN 96193613
TI The effect of leukotriene synthesis inhibitors in models of acute and
chronic inflammation.
AU Nickerson-Nutter C L; Medvedeff E D
CS Bayer Corporation, New Haven, Connecticut, USA.
NC AR-31133 (NIAMS)
SO ARTHRITIS AND RHEUMATISM, (1996 Mar) 39 (3) 515-21.
Journal code: 90M. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199607
AB OBJECTIVE: To assess the efficacy of leukotriene synthesis inhibitors,
alone and in combination with a nonsteroidal antiinflammatory ***drug***
, as potential treatments for ***rheumatoid*** ***arthritis***
(RA), using the mouse air pouch ***model*** and the collagen-induced
arthritis (CIA) ***model*** . METHODS: Two selective
leukotriene synthesis inhibitors, Bay x 1005 and Bay y 1015, were compared
with zileuton in terms of their ability to decrease exudate volume, cell
infiltration, and leukotriene B4 (LTB4) production in response to zymosan
injection in the mouse air pouch ***model*** . The mouse CIA
model was used to assess the effect of leukotriene synthesis
inhibitors in a ***model*** of chronic inflammation. Bay y 1015 and
Bay x 1005, and the cyclooxygenase inhibitor naproxen, were evaluated
individually and in combination, for their antiarthritic potency in the
mouse CIA ***model*** . RESULTS: The results indicate that neither
zileuton, Bay x 1005, nor Bay y 1015 inhibited exudate production. All 3
compounds decreased LTB4 levels in be air pouch, with Bay y 1015 being the
most effective. Cell infiltration was significantly decreased with Bay x
1005, but the degree of this decrease did not appear to correlate with
LTB4 levels. No inhibition of ***arthritis*** was observed with any
compound administered alone. In contrast, a significant inhibition of CIA
was observed in animals that received both naproxen and either Bay y 1015
or Bay x 1005. CONCLUSION: Inhibitors of both cyclooxygenase and
leukotriene synthesis in combination may be a more effective treatment of
RA than either class of inhibitors alone.

L25 ANSWER 16 OF 36 MEDLINE
AN 96331229 MEDLINE
DN 96331229
TI ***Therapeutic*** effect of the anti-Fas antibody on ***arthritis***
in HTLV-1 tax transgenic mice.
AU Fujisawa K; Asahara H; Okamoto K; Aono H; Hasunuma T; Kobata T; Iwakura Y;
Yonehara S; Sumida T; Nishioka K
CS Division of Rheumatology and Immunology, Institute of Medical Science, St.
Marianna University School of Medicine, Japan.
SO JOURNAL OF CLINICAL INVESTIGATION, (1996 Jul 15) 98 (2) 271-8.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199611
AB We have recently demonstrated Fas-mediated apoptosis in the synovium, of
patients with ***rheumatoid*** ***arthritis*** (RA) and suggested
that it may be one factor responsible for the regression of RA. To examine
whether the induction of apoptosis caused by anti-Fas mAb may play a
potential role as a new ***therapeutic*** strategy for RA, we
investigated the effect of anti-Fas mAb (RK-8) on synovitis in an

animal
model of RA, the human T cell leukemia virus type I (HTLV-1) tax
transgenic mice. We report here that administration of anti-Fas mAb into
mice intra-articularly improved the paw swelling and ***arthritis***
within 48 h. Immunohistochemical study and in vitro culture studies showed
that 35% of synovial fibroblasts, 75% of mononuclear cells, and some of
polymorphonuclear leukocytes infiltrating in synovium underwent apoptosis
by anti-Fas mAb. In situ nick end labeling analysis and electron
microscope analysis clearly showed that many cells in synovium were
induced apoptosis by anti-Fas mAb administration. However, local
administration of anti-Fas mAb did not produce systemic side effects.
Results demonstrated that administration of anti-Fas mAb in arthritic
joints of the HTLV-1 tax transgenic mice produced improvement of
arthritis . These findings suggest that local administration of
anti-Fas mAb may represent a useful ***therapeutic*** strategy for
proliferative synovitis such as RA.

L25 ANSWER 17 OF 36 MEDLINE DUPLICATE 3
AN 95367064 MEDLINE
DN 95367064
TI The antiinflammatory effects of an adenosine kinase inhibitor are mediated
by adenosine.
AU Cronstein B N; Naime D; Firestein G
CS New York University Medical Center, New York, NY, USA..
NC AR-10949 (NIAMS)
HL-19721 (NHLBI)
M01-RR-00096 (NCRR)
+
SO ARTHRITIS AND RHEUMATISM, (1995 Aug) 38 (8) 1040-5.
Journal code: 90M. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199511
AB OBJECTIVE. The acute antiinflammatory effects of methotrexate are
mediated, at least in part, by increased extracellular adenosine
concentrations at inflamed sites. This observation suggests that other
agents that increase extracellular adenosine concentrations might also
reduce inflammation. Since adenosine can be rapidly taken up by cells,
phosphorylated by adenosine kinase, and maintained intracellularly as
adenine nucleotides, we investigated whether a potent inhibitor of
adenosine kinase, GP-1-515, could increase exudate adenosine concentration
and thereby diminish inflammation in the murine air pouch ***model***
of inflammation. METHODS. We studied the effect of various oral doses of
GP-1-515 on carrageenan-induced inflammation in air pouches induced on
BALB /c mice. Adenosine concentration in pouch exudates was
determined by high performance liquid chromatography, and intensity of
inflammation was determined by leukocyte counts in the exudate fluid.
RESULTS. There was a greater concentration of adenosine in the pouch
exudates of animals treated with GP-1-515 than of those treated with
saline ($P < 0.002$). GP-1-515 inhibited, in a dose-dependent manner ($P <$
0.01), leukocyte accumulation in the murine air pouch in response to
carrageenan. Inhibition of inflammation by GP-1-515 in this ***model***
depended upon increased adenosine concentration in the inflamed pouch
since injection of adenosine deaminase into the air pouch with the
carrageenan completely reversed the antiinflammatory effects of GP-1-515
at all doses of GP-1-515 tested. Moreover, as previously demonstrated, the
antiinflammatory effects of adenosine were mediated via occupancy of
adenosine A2 receptors, since the specific adenosine A2 receptor
antagonist 3,7-dimethyl-1-propargylxanthine, but not the A1 receptor
antagonist 8-cyclopentyl-dipropylxanthine, completely reversed the
antiinflammatory effects of GP-1-515. GP-1-515 also decreased tumor
necrosis factor alpha levels in the air pouch exudates by 51%, most likely
as a result of the direct action of adenosine on macrophages.
CONCLUSION.
These results indicate that the antiinflammatory actions of GP-1-515 are
mediated by adenosine. The development of agents that promote adenosine
release at sites of inflammation is a novel strategy for the treatment of
inflammatory diseases such as ***rheumatoid*** ***arthritis*** .

L25 ANSWER 18 OF 36 MEDLINE
AN 95132631 MEDLINE
DN 95132631
TI Leukotriene B4 plays a critical role in the progression of
collagen-induced ***arthritis*** .
AU Griffiths R J; Pettipher E R; Koch K; Farrell C A; Breslow R; Conklyn M J;
Smith M A; Hackman B C; Wimberly D J; Milici A J; et al
CS Central Research Division, Pfizer Inc., Groton, CT 06340..
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
AMERICA, (1995 Jan 17) 92 (2) 517-21.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199504
AB Leukotriene B4 (LTB4) is a product of the 5-lipoxygenase pathway of
arachidonic acid metabolism. LTB4 is a potent chemotactic factor for
neutrophils and has been postulated to play an important role in a variety
of pathological conditions including ***rheumatoid***
arthritis (RA), psoriasis, and inflammatory bowel disease. The
role of LTB4 in such diseases has not yet been defined but in this paper
we provide direct evidence that LTB4 plays a critical role in a murine
model of RA. CP-105,696,
(+)-1-(3S,4R)-[3-(4-phenylbenzyl)-
4-hydroxychroman-7-yl]cyclopentane carboxylic acid, is an LTB4 receptor
antagonist that inhibits LTB4 binding to human neutrophil membranes with
an IC50 of 3.7 nM and inhibits LTB4-induced chemotaxis of these cells with
an IC50 of 5.2 nM. CP-105,696 inhibits LTB4-induced neutrophil influx in
mouse skin when administered orally with an ED50 of 4.2 mg/kg. CP-105,696
had a dramatic effect on both the clinical symptoms and histological
changes of murine collagen-induced ***arthritis*** when administered
at doses of 0.3-10 mg/kg. Inhibition was not associated with suppression
of the humoral immune response to collagen and was equally effective if
drug treatment was commenced just prior to the onset of
arthritis or throughout the experiment. These results suggest that
LTB4 receptor antagonists may be effective ***therapeutic*** agents
for the treatment of RA.

L25 ANSWER 19 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

AN 95238645 EMBASE
DN 1995238645
TI D-penicillamine-induced autoantibodies in a mouse ***model*** .
AU Brik R.; Tenenbaum G.; Blank M.; Shoenfeld Y.; Barzilai D.; Bloch K.;
Vardi P.
CS Pediatric Rheumatology, Department of Pediatrics, Rambam Medical
Center,Haifa, Israel
SO Clinical and Experimental Rheumatology, (1995) 13/4 (483-488).
ISSN: 0392-856X CODEN: CERHDP
CY Italy
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Objective. We have previously shown that the administration of
D-penicillamine (D-PEN) to patients with ***rheumatoid*** ***arthritis*** induces circulating insulin autoantibodies (INSAAB). In
order to gain further insight into such immune responses, we measured a
battery of circulating autoantibodies in 4 strains of mice receiving
D-PEN: C57BL/KsJ, ***BALB*** /c, C3H/HeJ, and C57BL/6. These rodents
groups differ in their degree of susceptibility to streptozotocin
(STZ)-induced immune diabetes (SIMD), which is high in the first 2
strains, and mild and nil in the third and fourth, respectively. Methods.
Randomly assigned animals from each group were given a weekly subcutaneous
(SC) injection of either D-PEN 1 mg, D-PEN 3 mg, or solvent (PBS) for
aperiod of 4 weeks. Serum levels of antibodies to insulin, single stranded
DNA (ssDNA), thyroglobulin, and cardiolipin were measured weekly. Results.
Only the C57BL/KsJ and C3H/HeJ mice reacted to D-PEN administration. When
compared to the pre-treated and solvent-treated mice, D-PEN 1 mg, and to a
lesser degree D-PEN 3 mg, induced elevation of antibodies to insulin and
to ssDNA in C57/KsJ mice ($p < 0.001$), while only ssDNA antibodies were
detected in the C3H/HeJ mice ($p < 0.0001$ for D-PEN 1 mg; $p < 0.05$ for
D-PEN 3 mg). D-PEN had no effect on the level of antibodies to cardiolipin
or to thyroglobulin in any of the mice. Conclusions. This study showed
that D-PEN induces an antigen(s)-specific humoral response only in mice
already inherently prone to autoimmunity. This ***model*** suggests
that the activation of autoimmunity by environmental factors is probably
facilitated by genetic background, and might partly explain the diversity
of autoimmune manifestations in D-PEN treated patients.

L25 ANSWER 20 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 95260650 EMBASE
DN 1995260650
TI Antigen-specific B cells present cartilage proteoglycan (aggrecan) to an
autoreactive T cell hybridoma derived from a mouse with
proteoglycan-induced ***arthritis*** .
AU Brennan F.R.; Mikecz K.; Buzas E.I.; Ragasa D.; Cs-Szabo G.; Negroiu G.;
Glant T.T.
CS Department Biochemistry, Rush-Presbyterian-St Luke's Med. Ctr, 1653 West
Congress Parkway,Chicago, IL 60612, United States
SO Clinical and Experimental Immunology, (1995) 101/3 (414-421).
ISSN: 0009-9104 CODEN: CEXIAL
CY United Kingdom
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
AB Cartilage proteoglycan (aggrecan)-induced polyarthritis in ***BALB***
/c mice is characterized by chronic inflammation and destruction of joint
tissues similar to that observed in human ***rheumatoid*** ***arthritis*** . The immunization of mice with fetal human proteoglycan
(PG) elicits specific antibodies to the immunizing antigen of which a
population cross-reacts with native mouse PG. This (auto)antibody
production is immediately followed by an explosive proliferation of
autoreactive T cells, suggesting that PG-specific B cells may participate
in antigen presentation of PG to autoreactive T cells. We therefore
isolated B cells from the spleens and lymph nodes of PG-immunized mice and
examined their ability to present PG to a PG-specific T cell hybridoma.
The antigen-specific T cell responses elicited by B cells from
PG-immunized mice (both arthritic and clinically asymptomatic) were
markedly higher than those of non-immune mice and keyhole limpet
haemocyanin (KLH)-immunized mice, and these B cells could present low PG
concentrations. Levels of B cell presentation corresponded with the serum
levels of PG-specific antibodies, implying that these B cells were
presenting the PG specifically via their surface immunoglobulin. This B
cell-T cell interaction was strongly dependent on MHC class II/T cell
receptor (TCR), LFA-1/intercellular adhesion molecule-1 (ICAM-1) and
CD28/B7 interactions, as antibodies to Ia, ICAM-1 and B7-2 (but not to
B7-1) markedly reduced presentation. These data indicate that PG-specific
B cells may play an essential role in governing the development of
PG-induced ***arthritis*** .

L25 ANSWER 21 OF 36 MEDLINE
AN 97005204 MEDLINE
DN 97005204
TI ***Therapeutic*** effects of antibodies against adhesion molecules in
murine collagen type II-induced ***arthritis*** .
AU Zeidler A; Brauer R; Thoss K; Bahnsen J; Heinrichs V; Jablonski-Westrich
D; Wroblewski M; Rebstock S; Hamann A
CS Abt. f. Immunologie, Universitatskrankenhaus Eppendorf, Hamburg, F.R.G.
SO AUTOIMMUNITY, (1995) 21 (4) 245-52.
Journal code: A5H. ISSN: 0891-6934.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
EW 19970204
AB Adhesion molecules play important roles in immune reactions and
inflammatory processes and may constitute attractive targets for
immunomodulatory approaches. In this study, blocking mAbs against a series
of adhesion molecules were tested for their ***therapeutic*** effect
on developing ***arthritis*** in a mouse ***model*** . MAbs were
given for a period of 4 weeks at the time of exspected incidence of
visible disease symptoms, i.e. 4 weeks after priming with collagen type
II. A significant reduction of incidence down to values of 13% and 29% of
the controls was obtained with mAbs against CD44 and alpha 4-integrin,
respectively, during an observation time of 13 weeks. MAbs against CD4 and
LFA-1 resulted only in weaker, non-significant effects or a delay in the

incidence. MAbs against other molecules including L-selectin, ICAM-1 or
VCAM-1 were not effective. The development of antibodies against collagen
type II, collagen type I, proteoglycans and the immunogen, bovine collagen
type II was affected by mAb treatment to a different extent. In this case,
the anti CD4 mAb was the most effective, followed by the anti alpha
4-antibodies in most cases, whereas anti CD44 showed less clear effects on
the development of humoral responses. In a skin delayed type
hypersensitivity ***model*** analyzed for comparison, mAbs against
LFA-1/ICAM-1 and alpha 4-integrin showed the largest effects on ear
swelling. These data show that mAbs against several adhesion molecules are
able to block selectively distinct aspects of immune reactions, and that
CD44 and alpha 4-integrins could be promising targets for an immunotherapy
of ***rheumatoid*** ***arthritis*** with receptor-interfering
agents.

L25 ANSWER 22 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 94357272 EMBASE
DN 1994357272
TI Induction of lupus-associated autoantibodies in ***BALB*** /c mice by
intraperitoneal injection of pristane.
AU Satoh M.; Reeves W.H.
CS Division of Rheumatology/Immunology, 932 FLOB, University of North
Carolina,Chapel Hill, NC 27599-7280, United States
SO Journal of Experimental Medicine, (1994) 180/6 (2341-2346).
ISSN: 0022-1007 CODEN: JEMEAV
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB Intraperitoneal injection of pristane (2,6,10,14 tetramethylpentadecane)
is a standard technique for obtaining monoclonal antibody-enriched ascitic
fluid. However, pristane also induces plasmacytomas and an erosive
arthritis resembling ***rheumatoid*** ***arthritis*** in
BALB /c mice, probably as a consequence of enhanced interleukin 6
production. We report here that the production of autoantibodies
characteristic of systemic lupus erythematosus (SLE) is a further
consequence of injecting pristane in ***BALB*** /c mice. Anti-Su
antibodies appeared as early as 1-2 mo after a single injection of 0.5 ml
pristane, followed by anti-U1RNP and anti-Sm antibodies after 2-4 mo.
Within 6 mo of pristane injection, 9 of 11 ***BALB*** /c mice had
developed anti-Su, anti-U1RNP, anti-U2RNP, anti-Sm, and possibly
anti-U5RNP antibodies. Autoantibodies were not produced by 20 ***BALB***
/c mice of the same age and sex that were not injected with pristane.
Thus, autoantibodies characteristic of lupus were induced in mice that are
not usually considered to be genetically susceptible to the disease. The
induction of autoantibodies associated with SLE by pristane may be
relevant to understanding the role of abnormal cytokine production in
autoantibody production and the pathogenesis of autoimmune disease.
Furthermore, the induction of high titer autoantibodies by pristane
dictates caution in the use of ascitic fluid as a source of monoclonal
antibodies, since the polyclonal autoantibodies induced by pristane may
copurify with the monoclonal antibody secreted by an injected hybridoma.

L25 ANSWER 23 OF 36 MEDLINE
AN 95043628 MEDLINE
DN 95043628
TI Cartilage contribution to gender differences in joint disease progression.
A study with rat articular cartilage.
AU Larbre J P; Da Silva J A; Moore A R; James I T; Scott D L; Willoughby D A
CS Department of Experimental Pathology, St Bartholomew's Hospital Medical
College, London, U.K..
SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY, (1994 Jul-Aug) 12 (4) 401-8.
Journal code: DFA. ISSN: 0392-856X.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199502
AB OBJECTIVE. ***Rheumatoid*** ***arthritis*** is associated with a
worse prognosis in females and is influenced by sex hormone changes.
Similar observations in osteoarthritis support the hypothesis that gender
differences in cartilage make a hitherto unrecognized contribution to
gender differences in ***arthritis*** . The aim of the present study
was to investigate potential gender differences in articular cartilage
biochemistry, metabolism and response to inflammatory mediators. METHODS.
Femoral head cartilages from age-matched male and female Wistar rats were
analysed for the water, glycosaminoglycan, hydroxyproline and collagen
crosslink contents. Proteoglycan loss and synthesis were assessed in
vitro, and in the presence and absence of serum and interleukin-1. An in
vivo ***model*** of inflammation-induced cartilage degradation was
employed to investigate gender differences in cartilage susceptibility to
erosion caused by granulomatous tissue. RESULTS. Articular cartilage from
male Wistar rats presented higher levels of both proteoglycan and collagen
and showed a lower spontaneous glycosaminoglycan loss and higher
proteoglycan synthesis in vitro than cartilage from females. Proteoglycan
synthesis from female, but not male, cartilage was significantly
stimulated by foetal calf serum. Female cartilage was more sensitive to
IL-1 inhibition of proteoglycan synthesis while the opposite was observed
in IL-1-induced proteoglycan loss. Female cartilage was more susceptible
to granuloma-induced degradation than male when implanted into female
mice, but no differences were observed between male and female cartilage
implanted in male mice. CONCLUSION. These results demonstrate important
gender differences in cartilage biochemistry, metabolism and
susceptibility to inflammatory mediators which may have important
consequences for the joint destruction in ***arthritis*** and support
a role for hormone ***therapy*** .

L25 ANSWER 24 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 4
AN 94268002 EMBASE
DN 1994268002
TI Suppression of autoimmune responses and inflammatory events by leflunomide
in an animal ***model*** for ***rheumatoid*** ***arthritis*** .
AU Glant T.T.; Mikecz K.; Brennan F.; Negroiu G.; Bartlett R.R.
CS Department of Biochemistry, Rush Med Univ Rush-Presbyterian-St, Luke's
Medical Center, 1653 West Congress Parkway,Chicago, IL 60612, United
States

SO Agents and Actions, (1994) 41/SPEC. ISS. II (C267-C270).
ISSN: 0065-4299 CODEN: AGACBH
CY Switzerland
DT Journal; Conference Article
FS 026 Immunology, Serology and Transplantation
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
AB The effect of leflunomide (HWA 486) was tested in proteoglycan-induced
arthritis in an autoimmune animal ***model*** showing many
similarities to human ***rheumatoid*** ***arthritis*** and
ankylosing spondylitis. The development of the disease in genetically
susceptible ***BALB*** /c mice is dependent upon the expression of both
cell-mediated and humoral immunity to host mouse cartilage proteoglycan.
Arthritic and control (non-arthritic) animals were treated with 35 mg
leflunomide/kg body weight/day for 12 weeks to suppress inflammatory
events and antibody titers. Leflunomide suppressed acute inflammatory
events, protected animals from new inflammatory episodes and acute
exacerbations, slightly reduced the stiffness in joints and blocked the
degradation of cartilage. The suppressive effect of leflunomide in
proteoglycan-induced ***arthritis*** is due primarily to the
suppression of autoantibody formation.

L25 ANSWER 25 OF 36 MEDLINE
AN 95044819 MEDLINE
DN 95044819
TI Prevention of spontaneous polyarthritis in NZB/KN mice by treatment with a
novel thiazole derivative, SM-8849.
AU Nishikaku F; Nakamura K; Kashiwazaki S; Koga Y
CS Research Laboratories, Sumitomo Pharmaceuticals Company, Osaka, Japan..
SO DRUGS UNDER EXPERIMENTAL AND CLINICAL RESEARCH, (1994) 20 (3) 85-92.
Journal code: EBM. ISSN: 0378-6501.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199502
AB NZB/KN mice spontaneously develop polyarthritis, characterized by
infiltration of inflammatory cells into the synovium and destructive damage of articular cartilage and bone. This study was performed to elucidate the effects of a novel thiazole derivative (SM-8849;
(4-[1-(2-fluoro-4-biphenylyl)-ethyl]-2-methylamino thiazole) in comparison
with the cyclooxygenase inhibitor, indomethacin, on disease development
and immune disorders in NZB/KN mice. Mice were treated with SM-8894 (50
mg/kg) or indomethacin (2 mg/kg), starting from two months of age, for
seven months. Indomethacin had no inhibitory effect on joint lesions in
this ***model*** . In contrast, SM-8849 was effective in arresting the
progression of ***arthritis*** , as confirmed by histologic and
radiographic studies. Moreover, SM-8849, but not indomethacin, suppressed
rheumatoid factor production. In addition, the population of CD5+
B cells in the peritoneal cavity and spleen was reduced with SM-8849
treatment. These findings suggest that NZB/KN mice are of use in the
evaluation of intrinsic antiarthritic activity, independently of
cyclooxygenase inhibition. Additionally, the ***therapeutic*** value
of SM-8849 is strongly suggested by its efficacy in this ***model*** .

L25 ANSWER 26 OF 36 MEDLINE
AN 93249323 MEDLINE
DN 93249323
TI Protective effect of androgens against inflammation induced cartilage
degradation in male rodents.
AU Da Silva J A; Larbre J P; Spector T D; Perry L A; Scott D L; Willoughby D
A
CS Department of Experimental Pathology, St Bartholomew's Hospital Medical
College, London, United Kingdom..
SO ANNALS OF THE RHEUMATIC DISEASES, (1993 Apr) 52 (4) 285-91.
Journal code: 62W. ISSN: 0003-4967.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199308
AB OBJECTIVES-- ***Rheumatoid*** ***arthritis*** (RA) is a disease
which predominantly affects women. Interestingly, low serum androgen
levels and clinical improvement with androgen replacement have been
reported in male patients. The aetiopathogenic role of sex hormones in
arthritis and their potential long term effects on joint destruction and disability remains unclear, however. This study was
designed to investigate the potential influence of sex hormones on inflammation induced cartilage degradation in male rodents.
METHODS--An in
vivo ***model*** of cotton wrapped cartilage implants was used to
assess the effects of androgen, oestradiol, and progesterone on inflammation induced cartilage degradation, and in vitro techniques were
used to investigate the direct actions on cartilage metabolism and cytokine production in male animals. RESULTS--Orchidectomy resulted in
accelerated cartilage damage which was reversed by replacement of physiological levels of androgens. Granulomatous tissue from castrated
male rodents produced higher amounts of interleukin 1. Sex hormones
reduced spontaneous proteoglycan loss in vitro but did not interfere with
the effects of interleukin 1 on cultured cartilage.
CONCLUSIONS--Androgens
appear to protect cartilage from inflammation induced breakdown in male
animals. These results support a pathogenic role for hypoandrogenism in
rheumatoid ***arthritis*** and suggest that long term androgen
replacement may help prevent joint damage and disability.

L25 ANSWER 27 OF 36 MEDLINE
AN 93058997 MEDLINE
DN 93058997
TI Pristane induced ***arthritis*** in mice. IV. Immunotherapy with
monoclonal antibodies directed against lymphocyte subsets.
AU Levitt N G; Fernandez-Madrid F; Wooley P H
CS Department of Internal Medicine, Wayne State University School of
Medicine, Detroit, MI..
SO JOURNAL OF RHEUMATOLOGY, (1992 Sep) 19 (9) 1342-7.
Journal code: JWX. ISSN: 0315-162X.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199302
AB Pristane induced ***arthritis*** (PIA), a seropositive experimental
disease ***model*** in mice, was used to investigate the influence of
immunotherapy with monoclonal antibodies against lymphocyte subsets.
Treatment with L3T4, a monoclonal antibody specific for murine CD4+ T
cells, significantly reduced the incidence of pristane ***arthritis***
, and delayed the disease onset. Monoclonal antibody to Lyt2, the murine

CD8+ T cell marker, significantly reduced the levels of ***rheumatoid*** factor in pristane injected animals compared with controls, but did not influence the clinical course of PIA. Our experiments demonstrate the ability of anti-CD4 antibodies to modify the course of PIA, and provide support for the hypothesis that CD4+ T lymphocytes have an important role in the pathogenesis of this experimental autoimmune ***arthritis*** .

L25 ANSWER 28 OF 36 MEDLINE
AN 93000344 MEDLINE
DN 93000344
TI ***Rheumatoid*** ***arthritis*** synovial fluid enhances T cell effector functions.
AU Ridderstad A; Abedi-Valugerdi M; Strom H; Moller E
CS Department of Immunology, Arrhenius Laboratories for Natural Sciences, University of Stockholm, Sweden..
SO JOURNAL OF AUTOIMMUNITY, (1992 Jun) 5 (3) 333-50. Journal code: ADL. ISSN: 0896-8411.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199301
AB ***Rheumatoid*** ***arthritis*** is a chronic autoimmune joint disease of unknown etiology. T cells are believed to be important in the pathogenesis of ***rheumatoid*** ***arthritis*** since they infiltrate the joints and express several activation markers, such as MHC class II and IL-2R. In this study we have elucidated the effect on freshly isolated T cells of ***rheumatoid*** ***arthritis*** synovial fluid (RA-SF), which contains in vivo produced cytokines and enzymes. The mouse mixed lymphocyte culture (MLC) has been used as a ***model*** and specific cytotoxicity was evaluated against 51Cr-labelled sensitive target cells. Studies have shown that RA-SF contains a B cell differentiation activity that can cross-react between the human and murine species. Here we have shown that the addition of RA-SF strongly potentiates cytotoxic activity as well as lymphokine production by allogeneic activated effector T cells. The enhanced cytotoxicity induced by RA-SF was found to be due to a combined effect of increased cytotoxic T lymphocyte (CTL) precursor frequency, measured by limiting dilution analysis, and a more efficient killing on a per cell basis. Kinetic studies show that RA-SF must be added within 48 h after initiation of the MLC, otherwise the effect is lost. The target cell specificity of RA-SF was studied, using enriched CD4+ or CD8+ responder cells in the MLC. It was found that RA-SF could act directly on the CD8+ cells and potentiate their development to cytotoxic effector cells: this activity was not found when CD4+ responder cells were used instead. RA-SF could, on the other hand, greatly enhance IL-2 production by CD4+ responder cells. We suggest that B and T cell activity in RA-SF is important in the propagation of chronic inflammation in the joints of patients with ***rheumatoid*** ***arthritis*** .

L25 ANSWER 29 OF 36 MEDLINE DUPLICATE 5
AN 92290784 MEDLINE
DN 92290784
TI Immunomodulation of proteoglycan-induced progressive polyarthritis by leflunomide.
AU Glant T T; Mikecz K; Bartlett R R; Deak F; Thonar E J; Williams J M; Mattar T; Kuettner K E; Schleyerbach R
CS Department of Biochemistry, Rush-Presbyterian-St.-Luke's Medical Center, Chicago, IL 60612..
NC AR 40310 (NIAMS)
SO IMMUNOPHARMACOLOGY, (1992 Mar-Apr) 23 (2) 105-16. Journal code: GY3. ISSN: 0162-3109.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199209
AB Proteoglycan-induced ***arthritis*** is a mouse ***model*** displaying many similarities to human ***rheumatoid*** ***arthritis*** and ankylosing spondylitis which has been documented by clinical and histopathological studies. The development of the disease in genetically susceptible ***BALB*** /c mice is dependent upon the expression of both cell-mediated and humoral immunity to host mouse cartilage proteoglycan. Since both development and regression of acute inflammatory processes in joints correlate directly with the serum antibody level to mouse cartilage proteoglycan, it is believed that these autoreactive antibodies may play a key role in the pathological mechanism of proteoglycan-induced ***arthritis*** . The treatment of arthritic animals with an immunomodulating agent (leflunomide) suppressed acute inflammatory events, protected animals from new inflammatory episodes or acute exacerbations in chronically inflamed joints and blocked pathological processes in arthritic joints, which otherwise led to progressive deformities, ankylosis and the loss of articular cartilage. We conclude that the suppressive effect of leflunomide (HWA 486) in proteoglycan-induced ***arthritis*** primarily is due to the suppression of autoantibody formation and that the ***drug*** may be a potential agent in human ***therapy*** as well. Further, we feel that this novel ***model*** of murine polyarthritis will extend further the pharmacological repertoire necessary to discover innovative antirheumatic ***drugs*** .

L25 ANSWER 30 OF 36 MEDLINE
AN 91237100 MEDLINE
DN 91237100
TI Defective neutrophil function in the autoimmune mouse strain MRL/lpr. Potential role of transforming growth factor-beta.
AU Gresham H D; Ray C J; O'Sullivan F X
CS Research Service, Harry S Truman VA Medical Center, Columbia, MO 65201..
NC AI-23790 (NIAID)
SO JOURNAL OF IMMUNOLOGY, (1991 Jun 1) 146 (11) 3911-21. Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199108
AB Patients with systemic autoimmune diseases such as SLE and ***rheumatoid*** ***arthritis*** have increased rates of morbidity and mortality caused by infection. Although this increased risk of infection has been primarily attributed to ***therapeutic*** immuno-suppression, some reports exist of defective polymorphonuclear leukocytes (PMN) function in these patients. The purpose of the present work is to investigate the recruitment of PMN phagocytic function in a murine ***model*** of autoimmunity, the MRL/lpr mouse.

PMN from
MRL/lpr, but not from congenic MRL/n mice, exhibit a marked defect in the
amplification of FcR-mediated phagocytosis stimulated by various inflammatory mediators. This defect is acquired and correlates with the
onset of the autoimmune disease observed in this strain. In addition,
MRL/lpr but not MRL/n PMN exhibit a defect in extravasation into the
thioglycollate-inflamed peritoneum. Incubation of MRL/n PMN in MRL/lpr
serum induces a defect in the amplification of PMN phagocytic function
identical to that observed with MRL/lpr PMN. The activity in the serum
that induces this defect is neutralized by an antibody to TGF-beta but not
by control antibodies. Incubation of murine and human PMN with purified
TGF-beta induces an identical defect in stimulated FcR-mediated ingestion.
In addition, TGF-beta-treated MRL/n PMN fail to extravasate into the
thioglycollate-inflamed peritoneum after injection into normal MRL/n
recipient mice. In addition, direct injection of TGF-beta into MRL/n mice
also reduces the percentage and number of PMN in the thioglycollate-
stimulated peritoneal exudates of these mice. The defect in PMN
extravasation and phagocytic function was not caused by failure of the
defective PMN to modulate the expression of the adhesion molecules, Mac-1
and Mel-14. These data indicate that defects in PMN function can be
observed in a murine ***model*** of autoimmunity and that spontaneous
production of TGF-beta possibly may play a crucial role in the
pathogenesis of the defective PMN function in this animal ***model*** .

L25 ANSWER 31 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 91249433 EMBASE
DN 1991249433
TI Gallium prevents adjuvant ***arthritis*** in rats and interferes with
macrophage/T-cell function in the immune response.
AU Matkovic V.; Balboa A.; Clinchot D.; Whitacre C.; Zwilling B.; Brown D.;
Weisbrode S.E.; Apseloff G.; Gerber N.
CS Department of Pharmacology, 5198 Graves Hall, Ohio State Univ. Coll. of
Med., 333 W. 10th Avenue,Columbus, OH 43210, United States
SO Current Therapeutic Research - Clinical and Experimental, (1991) 50/2
(255-267).
ISSN: 0011-393X CODEN: CTCEA
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The effect of gallium (Ga) nitrate on adjuvant ***arthritis*** was
studied in 24 male Lewis rats randomized into three groups: (1) Ga (30
mg/kg, then 10 mg/kg subcutaneously weekly) plus complete Freund's
adjuvant (n = 10), (2) vehicle (trisodium citrate) plus adjuvant (n = 8),
and (3) vehicle (n = 6). Rats received Ga or vehicle on day -1 and
adjuvant on day 0. Rats treated with adjuvant plus vehicle developed
arthritis , observed clinically in all limbs and measured by gait
impairment, performance on a rotobar, and blinded histological evaluation
of joints. Rats that had received Ga and adjuvant exhibited less prominent
clinical signs and significantly decreased histopathologic changes in
joints compared with those animals that received vehicle and adjuvant. The
effect of Ga in vitro on lymphoid cells was investigated using a
purified-protein-derivative-specific T-cell line derived from Lewis rats.
Ga completely suppressed the antigen-specific and mitogenic proliferative
responses. The effect of Ga on MHC class II expression by murine
macrophages was also studied. Peritoneal macrophages from ***BALB*** /c
mice were incubated with Ga after stimulation for 48 hours with
gamma-interferon to induce the expression of I-A glycoproteins. Ga
transiently reduced expression by approximately 45%. The effect of Ga on
macrophages and T-cell suggests that this agent may be useful in the
treatment of many autoimmune diseases and explains its protective effect
in adjuvant ***arthritis*** .

L25 ANSWER 32 OF 36 MEDLINE
AN 89140335 MEDLINE
DN 89140335
TI Heterogeneous effects of IFN-gamma in adjuvant ***arthritis*** .
AU Jacob C O; Holoshitz J; Van der Meide P; Strober S; McDevitt H O
CS Department of Microbiology, Stanford University School of Medicine, CA
94305.
NC AI-11313 (NIAID)
AI-07757 (NIAID)
SO JOURNAL OF IMMUNOLOGY, (1989 Mar 1) 142 (5) 1500-5.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198906
AB In an attempt to evaluate the role of IFN-gamma in autoimmune
arthritis , we tested the effects of IFN-gamma and anti-IFN-gamma
mAb (DB-1) in various phases of ***arthritis*** development in a rat
model for ***rheumatoid*** ***arthritis*** ; the adjuvant
arthritis (AA) ***model*** , induced by immunization with CFA.
In addition, the effects of IFN-gamma were tested in vitro on T cell
clones derived from rats afflicted with AA. T cell clone A2b, which has
been shown to be arthritogenic secreted low amounts of IFN-gamma and its
Ag-specific proliferation was inhibited by IFN-gamma. In contrast, clone
A2c, which can inhibit the development of AA, produced high amounts of
IFN-gamma and its proliferation was increased by IFN-gamma. In vivo
administration of IFN-gamma 24 h before CFA caused an enhancement of
arthritis , whereas giving IFN-gamma 24 to 48 h after CFA
suppressed the disease. Administration of IFN-gamma between day +4 to +12
or between day +12 to +24 increased the severity of the first phase of the
disease, but had no effect later. Administration of DB-1 1 to 2 days
before adjuvant or between day +4 to +8 substantially decreased the
disease, whereas DB-1 given from day +12 to +24 significantly enhanced it.
Taken together, these results illustrate the heterogeneity of IFN-gamma in
autoimmune ***arthritis*** and suggest a rational explanation for the
possibly conflicting reports regarding the role(s) and effects of
IFN-gamma in autoimmune processes. The multistage nature of T
cell-mediated autoimmune ***arthritis*** may be due to the
predominance of distinct T cell populations at different stages of the
disease. The differences in the biologic activities of these T cells may
be due to their patterns of lymphokine production.

L25 ANSWER 33 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 88091681 EMBASE
DN 1988091681
TI Immunopharmacological studies of new 3-benzoyl-4-mercaptobutyric acids. Immunomodulating effects.
AU Takeshita K.; Fukazawa I.; Futaki N.; Kameo K.; Tomisawa K.; Otomo S.; Aihara H.
CS Research Center, Taisho Pharmaceutical Co. Ltd., Saitama 330, Japan
SO Arzneimittel-Forschung/Drug Research, (1988) 38/4 (537-542). ISSN: 0004-4172 CODEN: ARZNAD
CY Germany
DT Journal
FS 030 Pharmacology
037 Drug Literature Index
031 Arthritis and Rheumatism
LA English
SL German; English
AB A number of D-penicillamine (PA) derivatives (3-benzoyl-4-mercaptobutyric acids) havinig acetylthio groups on an .alpha. or .beta. position of a carboxylic acid, were synthesized and examined for their immunological effects compared with PA. New PA derivatives suppressed adjuvant-induced ***arthritis*** (AA) in SD rats and enhanced AA in Lewis rats like PA. Suppressive effects of 2-acetylthiomethyl-3-(4-methyl-benzoyl)propionic acid (compound II-3) on AA in SD rats was most potent among PA derivatives and PA. II-3 enhanced type II collagen-induced ***arthritis*** in rats more effectively than PA, and it slightly prolonged the survival time of NZBXNZW hybrid (BWF1) mice. Hemolytic plaque forming cells in the spleen cells of BDF1 and aged ***Balb*** /c mice were potentiated but those of BWF1 were suppressed by both compounds. In in vitro experiments, both compounds enhanced lymphocyte transformation. On the contrary, II-3 had no effect on the acute inflammatory response, delayed type hypersensitivity and IgE antibody response. The abnormal release of lysosomal enzymes from the peritoneal macrophages of aged MRL/l mice were suppressed by both compounds. These results suggest that II-3 is an immunmodulator like PA but more effective than PA. II-3 may be clinically effective for ***rheumatoid*** ***arthritis*** .

L25 ANSWER 34 OF 36 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 89076304 EMBASE
DN 1989076304
TI Long-term ***therapeutic*** study with a new antirheumatic ***drug*** (CGS10787B) in MRL/I Mice.
AU Akita S.; Abe C.; Hirose S.
CS Biological Research Laboratory, Preclinical Research Department, R & D Subdivision, Pharmaceutical Division, Ciba-Geigy Japan Ltd., Takarazuka 665, Japan
SO International Journal of Immunotherapy, (1988) 4/3 (131-135). ISSN: 0255-9625 CODEN: IJIMET
CY Switzerland
DT Journal
FS 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LA English
SL English
AB MRL/Mp-lpr/lpr (MRL/I) mice are widely known to be poor inducers of interleukin-2 (IL-2) with low response to IL-2, and have been used for the study of systemic lupus erythematosus and ***rheumatoid*** ***arthritis*** . The long-term ***therapeutic*** effect of CGS10787B on the autoimmunity with lymphoproliferation in MRL/I mice was investigated. Mice were administered CGS10787B at doses of 25 and 100 mg/kg/day p.o. between 8 to 20 weeks of age. CGS10787B at a dose of 100 mg/kg prevented the lymphoproliferation of spleen and some lymph nodes in MRL/I mice. There were not any obvious changes in T-cell subsets in CGS10787B-treated mice. Although CGS10787B has no effect on excessive proteinuria in MRL/I mice, CGS10787B reduced high levels of serum anti-ssDNA antibody and IgG ***rheumatoid*** factor dose-relatedly. The effect of CGS10787B on IL-2 induction in ***BALB*** /c mice in vivo and MRL/I mice in vitro was also examined. While CGS10787B caused a slight reduction of IL-2 induction in ***BALB*** /c mice, a moderate increase in IL-2 induction in MRL/I mice was demonstrated. These findings on the ***therapeutic*** effect of CGS10787B on autoimmunity, polyclonal antibody formation and IL-2 induction in MRL/I mice suggest that CGS10787B would be useful for the treatment of rheumatic disease in man.

L25 ANSWER 35 OF 36 MEDLINE
AN 87036661 MEDLINE
DN 87036661
TI The effect of low dose chronic intermittent parental methotrexate on delayed type hypersensitivity and acute inflammation in a mouse ***model*** .
AU O'Callaghan J W; Bretscher P; Russell A S
SO JOURNAL OF RHEUMATOLOGY, (1986 Aug) 13 (4) 710-4. Journal code: JWX. ISSN: 0315-162X.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198702
AB We have shown that a regimen of low dose intermittent methotrexate (MTX), analogous to that used in the treatment of patients with ***rheumatoid*** ***arthritis*** , does have immunosuppressive effects on the induction of primary delayed type hypersensitivity in normal mice. This occurred even when the last MTX injection was 4 days before immunization. No effect was seen on established delayed type hypersensitivity or on inflammatory responses induced by carrageenan or the Arthus reaction.

L25 ANSWER 36 OF 36 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1986:213778 BIOSIS
DN BA81:105078
TI FAILURE OF METHOTREXATE AND METHYLPREDNISOLONE TO ALTER THE CLEARANCE OF ***MODEL*** IMMUNE COMPLEXES.
AU SCHRIBER L; MULLINS W W JR; PLOTZ P H
CS DEP. RHEUMATOLOGY, ROYAL NORTH SHORE HOSPITAL, ST LEONARDS, NSW 2065, AUSTRALIA.
SO J RHEUMATOL, (1985 (RECD 1986)) 12 (6), 1044-1047. CODEN: JRHUA9. ISSN: 0315-162X.
FS BA; OLD
LA English
AB We evaluated the effect of methotrexate (MTX) and methylprednisolone (MP) on reticuloendothelial system (RES) clearance of soluble ***model*** immune complexes (IC) in ***BALB*** /C mice. MTX was administered by intraperitoneal route either as a single dose (0.5 mg/kg) or as 10 alternate day doses (0.1 or 0.5 mg/kg), MP as a single intravenous (IV) bolus (50 mg/kg) with normal saline used as a control. Mice were then injected IV with radiolabeled IgG anti-DNP covalently crosslinked IC. Blood radioactivity was measured over a 3 h period at which time organ

utpake, corrected for blood contamination, was determined. Clearance
curves for each mouse were derived using the Marquardt-Levenberg curve
fitting method. No significant differences in IC clearance or organ uptake
were found between ***drug*** and control groups at any ***drug***
dose or time period. Our findings argue against an influence of MP and MTX
on immunospecific clearance of soluble IC.

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L1 16359 S BREEDING/AB,BI
L2 139 S L1 AND BALB?/AB,BI
L3 5 S L2 AND TRAIT#/AB,BI
L4 35308 S RHEUMATOID ARTHRITIS/AB,BI
L5 9 S L4 AND BREED?/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 13:57:45 ON 25
JUL 2000
L6 34 S L5
L7 21 DUP REM L6 (13 DUPLICATES REMOVED)
L8 7 S L7 AND BREEDING/AB,BI
L9 12601 S ARTHRITIS AND MODEL/AB,BI
L10 3695 S L9 AND (MICE OR MOUSE)/AB,BI
L11 20 S L10 AND PROGENY/AB,BI
L12 9 DUP REM L11 (11 DUPLICATES REMOVED)

FILE 'MEDLINE' ENTERED AT 14:04:55 ON 25 JUL 2000
L13 272 S RHEUMATOID ARTHRITIS AND SCREENING/AB,BI
L14 76 S L13 AND THERAP?/AB,BI
L15 9 S L14 AND MODEL/AB,BI
L16 69950 S BALB?/AB,BI
L17 368 S L16 AND ARTHRITIS/AB,BI
L18 79 S L17 AND MODEL/AB,BI
L19 43 S L18 AND RHEUMATOID/AB,BI
L20 0 S L19 AND SCREEN?/AB,BI
L21 1 S L18 AND SCREEN?/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 14:09:35 ON 25
JUL 2000
L22 1 S L21
L23 125 S L19
L24 44 S L23 AND (DRUG# OR THERAP?)/AB,BI
L25 36 DUP REM L24 (8 DUPLICATES REMOVED)

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